THE AMERICAN JOURNAL OF ROENTGENOLOGY
RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 67 APRIL, 1952 No. 4

# CRANIAL CLUES TO INTRACRANIAL ABNORMALITY

## CALDWELL LECTURE, 1951*

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## INTRODUCTION

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Mr. President:

You have conferred upon me a most signal honour in the request that I introduce the Caldwell Lecturer to the American Roentgen Ray Society tonight. To present an illustrious colleague, one's wartime chief and a revered associate in professional and academic life to you, my long-time friends in the Society and their guests, is a most happy occasion. His familiar name to some of us is "Wide," which denotes most graphically the diversity of his interests and talents.

Wilder Graves Penfield, son of a surgeon and a native of the Pacific Northwest, in the days before college football became a commercial enterprise in public entertainment, demonstrated at Princeton University that a good football player and a coach could also be an able scholar, with the result that he proceeded to Oxford University as a Rhodes scholar (in 1914), where he earned another bachelor's degree in 1916.

In his Princeton days, with several of his fellow students, Penfield was instrumental in the origin of the movement to draft Woodrow Wilson, then President of the University, for nomination as President of the United States.

The remaining First World War years were crammed full with his service as a "dresser," later as a surgeon in the Red Cross Hospitals in France, the completion of his degree in medicine from Johns Hopkins University and, possibly most importantly, as a sequel to being torpedoed in the English Channel, convalescence in the home of Sir William and Lady Osler.

During his Oxford days he was closely associated with Sherrington and Cuthbert Bassett. The story is told that one day, after operating upon a chimpanzee, Sherrington and Penfield carefully locked the door behind them. Then wondering what the "chimp" might be doing, they returned to peer through the keyhole, only to find his eye looking out at them.

* Delivered at the Fifty-second Annual Meeting of the American Roentgen Ray Society, Washington, D. C., September 25–28, 1951.

Extensive further post-graduate studies in surgery, neurology, neuropathology and neurophysiology as Beit Memorial Fellow, and in other appointments, included surgical services at the Peter Bent Brigham Hospital, St. Bartholomew's in London, and in Edinburgh; exceptional opportunity to work with del Rio Hortega, and particularly Ramon y Cajal in Spain, and with Foerster in Breslau.

Some of these preceded, and others were interspersed with his clinical and research duties as Associate Attending Surgeon to the Presbyterian Hospital, Assistant Professor of Surgery at Columbia, Assistant Surgeon to the Neurological Institute of New York and his Canadian career.

In 1928, largely through the foresight of the late great Canadian surgeon, Dr. Edward L. Archibald, Dr. Penfield was invited to occupy a new Chair in the Faculty of Medicine at McGill University as Professor of Neurology and Neurosurgery, and to be the Neurologist and Neurosurgeon-in-Chief of the Royal Victoria Hospital. Six years later, the Montreal Neurological Institute was completed. In this center for Canada, and in some measure internationally, Dr. Penfield, with his colleagues, has made major advances in the diagnosis and treatment of neurologic disease and research in neurophysiology and neuropathology, to which graduate students and distinguished physicians and surgeons come from all over the world. In the organization and operation of the Institute, Dr. Penfield and his associates have done much to enhance the entente cordiale between the French and English speaking members of our profession.

His career in Canada has also included distinguished public service, especially on the National Research Council. During the recent world war, I had the privilege of serving under him on the Sub-Committee for Surgery of the Associate Committee on Medical Research. His wide knowledge, personal charm and diplomacy ironed out many difficult problems, and made him the natural choice to represent the National Research Council of Canada and the Canadian Government following the unfortunate accidental death of Sir Frederick Banting.

While on a mission which included not only a visit to the Russian front and study of its wartime medical organization, but eastward to China and a conference with Generalissimo Chiang Kai-shek, Dr. Penfield took advantage of a forced delay of his air flight in the Middle East to pursue his interest in biblical and ancient history by a trek to the site of Ur of the Chaldees.

As a mark of appreciation of his services, Dr. Penfield was created a Companion of the Order of St. Michael and St. George by the King in the Birthday Honours of 1943.

Mr. President, I could go on for some time recounting our Lecturer's many other honours, among which are Chevalier de la Légion d'Honneur, Fellow of the Royal Society, Fellow of the Royal College of Surgeons of England, Fellow and sometime President of the Royal College of Surgeons of Canada, former President of the Association for Research in Neurological and Mental Diseases, President of the American Neurological Association, Fellow of Merton College (Oxford), Dunham Lecturer of Harvard University, Thayer Lecturer of Johns Hopkins University and recipient of the Medal of Freedom of the United States Government.

His ability in research, especially in neurophysiology and in the surgical correction or amelioration of organic disease of the nervous system, is internationally known.

But it is the man, father of four charming people (and grandfather of several), with gracious humility despite his many honours, the kindly physician who will spare much of his busy time to listen to his patient's story, or to reassure both patient and family; the teacher, not only of the undergraduate and graduate student, but in neuroradiology of those of us who have been privileged to work with him; and the colleague whom I would have you know and appreciate, as do his students and colleagues.

Mr. President, members of the Society and guests: Dr. Wilder Penfield.

## CALDWELL LECTURE

IT IS a great honour to stand before this venerable Society as Caldwell Lecturer. I thank President Kerr for this opportunity and Dr. Peirce for his generous introduction. In the impressive list of lecturers, I find the names of men of great renown in physics and medicine. From some of them I have myself drawn inspiration—Forssell, Cannon, Alvarez, Graham; and I take courage in the fact that my one-time colleague,

Merrill Sosman, has delivered one of the best in this succession of brilliant addresses.

At the outset, let me say that my friend, Dr. William Francis, who is curator of the Osler Library at McGill University, bids me place before you a claim to priority in the history of radiology. This claim, which, I hope, will not lead me into the quicksands of historical debate, is as follows:

The earliest recorded x-ray photograph made for the purposes of surgical diagnosis was taken by John Cox, Professor of Physics at McGill University, for Dr. R. C. Kirkpatrick, Lecturer in the Department of Surgery, on February 7, 1896.

Wilhelm Röntgen had communicated the discovery of what he called the X ray to the Academy of Würzburg on December 28, 1895. The news came out by ship and reached Montreal on February 5, 1896. Only two days later, February 7, a patient who had a bullet in his leg was placed under a Crookes tube in Professor Cox's laboratory. The resultant x-ray plate demonstrated the bullet *in situ*.

This was reported to the Montreal Medico-Chirurgical Society *the same night*, and the result was demonstrated in triumph so that all agreed that they could see the bullet. It is stated that, unfortunately, the plate was somewhat "underexposed," only forty-five minutes. They had hoped to keep the patient still for ninety minutes, but at the end of half that time the poor fellow is said to have become unreasonable and could not be controlled. The following day Dr. Kirkpatrick admitted him to the Montreal General Hospital and removed the bullet which had thus been localized.

All of this is reported in the *Montreal Medical Journal* of March, 1896, under the title of "The New Photography." Such was the speed of scientific recording in Montreal during "the nineties"! But, unfortunately, the print which appears in the report does not seem to show the bullet to my untrained eye. This is due, no doubt, to the shockingly short time of exposure.

It was two years later that the great pioneer of roentgenology whom we honour tonight bought a photographer's outfit and found that it included a roentgen-ray machine. He seems to have recognized at once how valuable this ray could be to medicine. But, alas, like other pioneers, he did not suspect the threat it held to his own life. The result was that after twenty years of constructive and exciting work, Eugene Wilson Caldwell died, a martyr to science. But he had helped to open a new field and to establish a unique and most important medical specialty. I hope he could pay his forfeit gladly, realizing the long-time importance of his work.

### A. PROLOGUE

Today the men who make up this specialty form a group apart. They are physicians. Some of them are physicists as well. But they spend their lives studying clues, clues to disease in other men's patients, and as a result all physicians and surgeons, great and small, bring them their problems. Radiologists form the great body of medical detectives. They seem to have the uncanny insight of Sherlock Holmes. Some that I have known even share his idiosyncrasies.

While Röntgen was working with Crookes tubes in the Physics Laboratory at Würzburg, a young and hopeful ophthalmologist, Dr. Arthur Conan Doyle, sat in his recently rented London consulting rooms, just around the corner from Harley Street, waiting for the patients who did not come. His mind turned back to the intriguing memory of one of his former teachers in Edinburgh, Mr. Joseph Bell. He recalled how, during his clinics at the Royal Infirmary, this surgeon would gather clues as he talked to each patient, unsuspected clues to his past life as well as to his present ailment.

I fancy that in the silence of his consulting room Dr. Doyle said to himself: "Disease is crime, the diagnostician a detective. . . . And Crime is disease. The detective is a diagnostician. To understand clues: that is the secret of success, in both professions."

Then he heard the sound of horses' hoofs outside the window. It might mean that a patient was coming to ask his advice. But the door did not open. Instead, the figure of a man appeared before Dr. Doyle—tall, stooped, aquiline, ascetic. Pipe, dressing-gown and nonchalance could not hide the amazing vigor of mind and of body which this man possessed. He was followed by another figure, a practitioner of medicine, Dr. Watson—an inquisitive little man, stolid and stupid perhaps, but loyal and easily forgiven.

A knock comes at the door. Dr. Doyle's consulting room seems to have changed into the lodgings of Sherlock Holmes at 221 B Baker Street. Mrs. Hudson enters with a letter. Dr. Doyle, now somewhat confused, casts a glance at Holmes who is stretching his feet toward the fire. Then he opens the letter and reads—"Ha!" It is a problem to be solved, a thrilling adventure that will lead them out into the life of London.

Sherlock Holmes gets up. He crosses to the fireplace. He takes tobacco out of a Persian slipper and, lighting his pipe, he fills the room with the haze of romance and reason, while Dr. Doyle (or is it Dr. Watson?) escapes from reality, the reality of hum-drum practice.

He is not sure, now, why he is waiting. Is it for a patient who is crossing Devonshire Place or is it for the sound of a mysterious hansom cab coming along Baker Street? He is not quite sure, either, whether he would prefer to pursue the clues of disease of the trail of that greatest of all criminals, Professor Moriarty.

In this lecture hall, I cannot pretend to the insight of a detective in radiology. But allow me, for the remainder of the hour, to look over your shoulders at the x-ray viewing box, while I talk, like Dr. Watson, about the history of the cases—and the physiology and pathology of growth and disease which account for the clues that your practiced eyes detect in the shadows of the roentgen ray.

### B. MATERIAL

Much has been written about the roentgen findings in cases of expanding lesions of the intracranial cavity, much about the findings in the diffuse diseases of the brain, about ventriculography and arteriography. Instead of discussing these things, I shall direct your attention to other conditions of the brain, meninges and skull, particularly those which have proved to be important in cases of focal cerebral seizures or focal epilepsy.*

### C. THE EPILEPTIC FOCUS

In all cases of recurring epileptic seizures the first duty of the clinician is to search for the cause of the attacks. He must eventually come to some classification of each case. Either he is dealing with idiopathic (cryptogenic, essential) epilepsy, which is due to unkown cause, or he is dealing with symptomatic epilepsy. In the first group the origin of the recurring epileptic discharges is usually deep in the higher brain stem in what may be called the centrencephalic neurone system that unites the two hemispheres into a functional unit. In such cases no objective lesion is at present demonstrable.

In the second group the focus of discharge is in an area of abnormal gray matter in one or the other hemisphere. This produces focal epilepsy, or better—focal cerebral seizures. In the great majority of cases the focus lies in the cerebral cortex of one hemisphere, and an objective lesion can very often be demonstrated. If the focus is situated in or near the rolandic sensory and motor cortex, the attacks are easily recognizable as jacksonian. But much more often the origin is hidden away in other regions of the cortex, and the localization by means of study of the seizure pattern may not be so obvious.

* It would have been quite impossible for me to collect the large number of cases restudied in the preparation of this address without the generous and enthusiastic assistance of Dr. Robert Aquilina of Beirut and Montreal.

To Dr. Donald McRae I am, as always, deeply indebted for his tolerant radiological guidance during this Watsonian excursion into the field of radiology.

Every patient who suffers from cerebral seizures of any sort should have roentgenograms made of his skull. This is the radiologist's opportunity of look for evidence of a brain lesion, asymmetries of skull and ventricles, calcifications, erosions. He may discover clues to the existence of an atrophic lesion of the brain or an expanding lesion of the intracranial cavity. But it will most often be the former.

Fits are produced by an abnormal state in the living gray matter. They do not arise in tumors, cysts, or fluid collections, nor in gray matter that has been destroyed and is no longer present. Epileptic discharge originates most often in the zone of living brain that may border such abnormalities.

A very large group of epileptics suffer from temporal lobe epilepsy. The electroencephalographer may record brain waves of four to six per second and may classifty them as psychomotor. Many of these patients have a focus in one or the other temporal lobe, and the radiologist should search carefully for abnormalities or asymmetries of the middle fossae of the skull.

The neurosurgeon who would treat focal epilepsy by radical cortical excision must study each case by every means available. When he has made a reasonably accurate localization he may hope to stop the seizures completely in a little over 50 per cent of the cases and decrease the attacks in others.

### D. CRANIAL ASYMMETRY

The human skull yields to the normal outward push of the growing brain during infancy and earliest childhood. At this period, therefore, brain injury or brain destruction results in overlying cranial smallness. The rate of growth is astonishingly rapid at first for the brain increases from an average weight of 300 gm. at birth to 500 gm. at six months. At two years the weight may normally reach 900 gm., and at puberty 1,200 gm., after which there is ordinarily an increase of no more than 100 gm.

Localized ischemic compression of the brain at birth results in ipsilateral cranial smallness. The overlying bone may come to be thickened and a little denser than on the opposite side. In such cases the falx gives the impression of having migrated across toward the injured side even at times when the head appears on inspection to have a normal shape (Fig. 1).

In later childhood, when paranasal sinuses and mastoid air cells make their appearance, they sometimes grow larger on the affected side, and the petrous pyramid and floor of the middle fossa seem to rise as though Nature were doing her best to hide this failure of brain growth from becoming apparent to any one except a radiologist.

In cases of small hemicranium, various types of lesion will be discovered in the hemisphere on the side of the smallness. The abnormality may be in an area of shrivelled gyri, or there may be single scattered atrophic convolutions. Such lesions may result in epileptic attacks years after birth (see Case M. M., Fig. 2, 3 and 4).

A subdural hematoma at birth may well disappear leaving only the adhesions between dura and arachnoid to tell the story but leaving also a portion of that hemisphere which does not grow.

There may be occlusions of large arteries at birth, and sometimes the evidence suggests that the occlusion may have occurred even before birth. As a result of these arterial blocks, a large zone of one hemisphere may be destroyed. In such a case, if fits occur, the cause will be found in the shrivelled gyri that almost invariably lie between the area of complete destruction and the comparatively normal brain. In Case C. P. (Fig. 5) the occipital end of the brain was thinned out to the proportion of a sack about the ventricle, but the epileptic focus lay in small gyri between this zone of destruction and the normal cortex anteriorly.

Often a cyst appears within the brain. It it does not communicate with the ventricle, the oxygen injected at the time of encephalography may fail to demonstrate it.

Fig. 1. Case N. P., aged eighteen. (Referred by Dr. Sylvio Caron, Quebec.) Small right hemicranium. Large right frontal sinuses. Birth injury and subdural hematoma, focal seizures beginning at six months. Left arm and leg were smaller and weaker than those on the other side. Marked atrophy of posterior half of the right hemisphere. Normal brain anterior to the central fissure. Radical excision.

Growth of the rest of the body, excepting only the brain and head, is controlled to some extent by the central nervous system. An early lesion of the postcentral gyrus produces smallness of that part of the contralateral half of the body which is represented in the injured area and that alone. This is shown in the case of D. H. (Fig. 6 and 7). This young woman had complete destruction of parietal and posterior frontal cortex on the left.

The degree of this smallness produced by cortical lesions is apt to be less than that produced by a contralateral infantile lesion of the gray matter of the spinal cord.

Perhaps the most frequent and certainly the most difficult natal lesion to identify is that produced by ischemia of one temporal lobe. There may be no more than a little smallness of the middle fossa, a little enlargement of the temporal horn of the ventricle on that side.

Patient J. Mc. had a clear focus in that area of the left temporal lobe that lies next to the incisura of the tentorium. This is the zone most frequently compressed at time of birth (Fig. 8 and 9).

### E. Ventricular Changes Produced by Atrophic Lesions

1. *Infantile Atrophic Lesions.* In some cases the ventricle on the side of the lesion is very large; in others, it shows little change. It is not always easy to explain the difference.

Partial ischemia at birth, which results in an area of microgyri, is apt to produce little change in the ventricle. The affected hemisphere is small. The normal gyri move toward the affected area during the active growth period. They seem to shoulder against their puny atrophic brothers so that at times the latter actually disappear below the surface.

Then, although cranium and hemisphere are reduced in volume, the ventricle may assume a roughly normal size and shape. If there is progressive atrophy after the period of active growth is past (and this does occur in many cases of focal epilepsy), then the ipsilateral ventricle shows varying degrees of progressive enlargement. On the other hand, early intracerebral hemorrhage

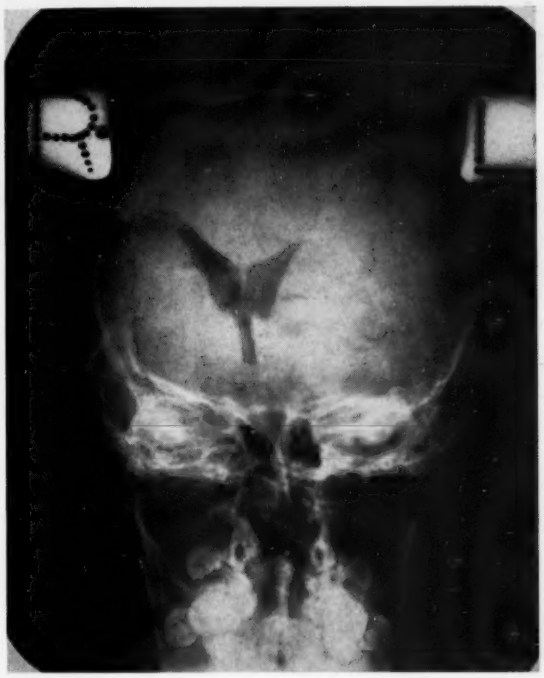

Fig. 2. Case M. M., aged seven. (Referred by Dr. A. Jimenez, Bogota.) Small right hemisphere, brain cyst and area of microgyri. Birth difficult, early feeding sluggish, focal cerebral seizures beginning at five years. Smallness of left side of body, good intelligence.

or occlusion of a large cerebral artery which completely destroys a zone of the hemisphere results in great enlargement of the corresponding ventricle.

2. *Adult Atrophic Lesions.* After the period of brain growth the skull has a relatively fixed size and shape. Atrophic lesions, acquired after that time, regularly produce enlargement of the adjacent ventricle. A striking characteristic of ventricular change in the adult is that one ventricle is rarely altered by an atrophic process without the

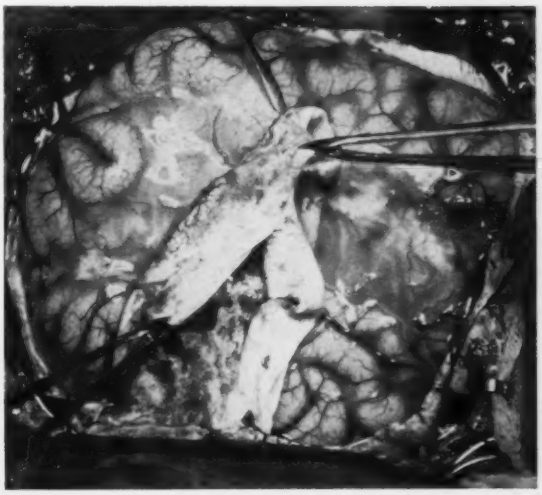

Fig. 3. Case M. M. Craniotomy. The dura is adherent because of subdural hematoma. Shrivelled gyri in central zone surrounded by normal appearing gyri. A "spike focus" was shown by electrocorticography in abnormal border.

appearance of a similar reflected change in the opposite ventricle. The reflected change is less in degree but similar in character.

This is, of course, the reverse of what happens as the result of expanding lesions.

Fig. 4. Case M. M. Excision of abnormal gyri down to white matter and forward to fissure of Rolando. The numbered tickets have been placed on the precentral gyrus when electrical stimulation produced positive responses, some of which were as follows: *2*, inversion of left foot; *10*, movement of great toe; *8*, flexion of wrist; *4*, movement of left thumb and index finger. No postoperative attacks up to present time, six months.

Fig. 5. Case C. P., aged twenty-one. (Referred by Dr. Jean Saucier, Montreal.) Small right hemicranium. Focal seizures began at age of seven. Destruction of occipital lobe as result of probable arterial closure at time of birth. Weakness and smallness of left arm and leg, left homonymous hemianopsia.

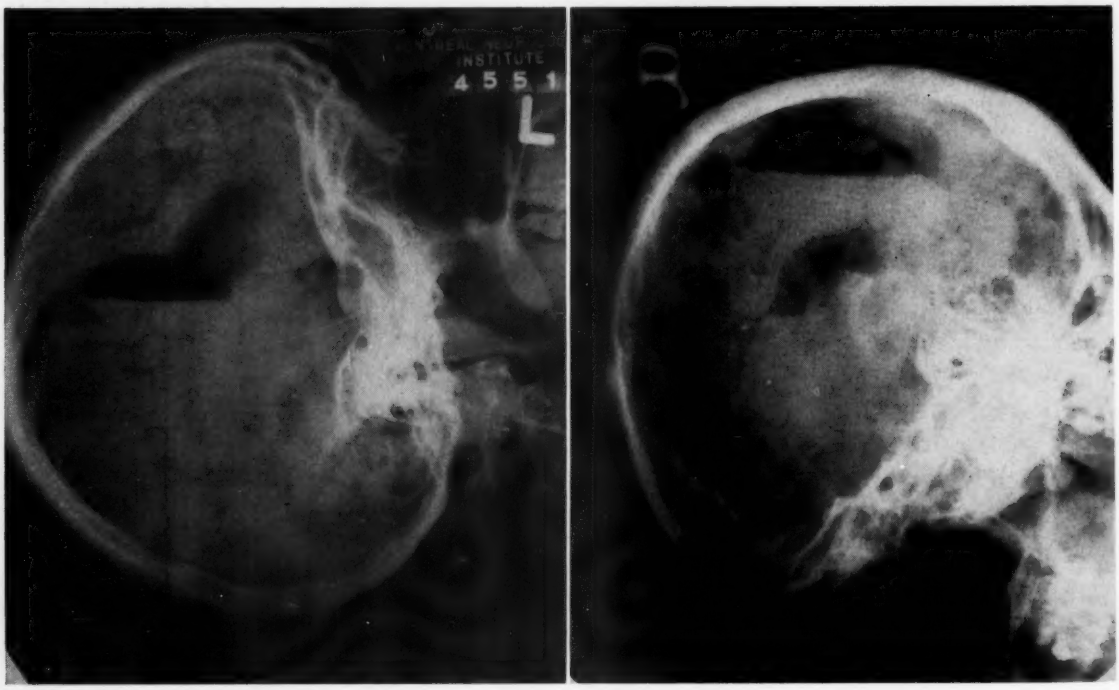


Fig. 6. Case D. H., aged twenty-five. (Referred by Dr. H. H. Blaustone, Austin, Texas.) Marked destruction of posterior and central portions of the left hemisphere as shown by enormous enlargement of that portion of ventricle due to birth injury with subdural hematoma. Focal cerebral seizures from fourteen months. Two epileptogenic foci were found and radical excision carried out.

Fig. 7. Case D.H. Smallness of right side of body, including foot, arm, breast, shoulder and face, due to severe lesion which included whole right postcentral gyrus.

In such cases direct compression of one ventricle decreases its size but produces distention of the opposite ventricle because of comparative obstruction of the aqueduct of Sylvius as it passes through the incisura of the tentorium.

Let me take as an example the case of H. M. He was a healthy, athletic man of fifty years who suffered a sudden complete left hemiplegia. The diagnosis was coronary thrombosis and cerebral embolism. Presumably there was no functional disturbance of the left hemisphere, for speech and movement of the right arm and leg were not affected.

Ten years afterward his left arm was still paralyzed and the left leg was nearly so. A pneumogram at that time showed diffuse enlargement of the right lateral ventricle and a large cyst in the central area of the right hemisphere. But there was also considerable enlargement of the left lateral ventricle as well. It was less in degree but similar in form. This is shown in Figure 10.

Various explanations of this phenomenon, which we may call reflected enlargement, might be suggested It may be argued that it is due to temporary edema of the brain which produces transient obstruction of the subarachnoid spaces and consequently a transient hydrocephalic dilatation of both ventricles.

It may be pointed out that any grave insult to one hemisphere produces an altera-

tion in the blood-brain barrier in that hemisphere and in the other hemisphere also. It is true that intravital dyes injected into the blood stream at such times will pass into the cerebral tissue on the two sides whereas they do not pass the barrier under normal conditions.

It may well be argued also that destruction of a large zone of gray matter in one hemisphere must, of necessity, cause degeneration of many collateral nerve fibers that cross in the corpus callosum to the homologous areas of cortex in the opposite hemisphere. This might produce a mirror-area of atrophy.

Whether it is produced by one mechanism or by a number of mechanisms, it is well to remember that an atrophic lesion of one hemisphere seems to produce what might be called *reflected contralateral ventricular enlargement.*

### F. CALCIFICATIONS

In cases of focal epilepsy intracranial calcification may be encountered in a variety of conditions.

All of the slowly growing brain tumors may undergo calcification and in some the patient may complain of seizures with no clinical evidence of increasing intracranial pressure. The pattern of calcification is not characteristic for each type.

Tuberculomas and healed brain abscesses of other types may show rather dense calcification.

There is a peculiar calcifying epileptogenic lesion of the cerebral cortex that is difficult to classify. The vessels at its center are apt to be largely thrombosed and it may seem avascular. We have called it hemangioma calcificans.[1] It makes its appearance most often in the temporal lobe. Pneumography usually gives slight evidence of expansion but occasionally it shows none. The lesion remains *in situ* year after year without change while the focal cerebral seizures continue.

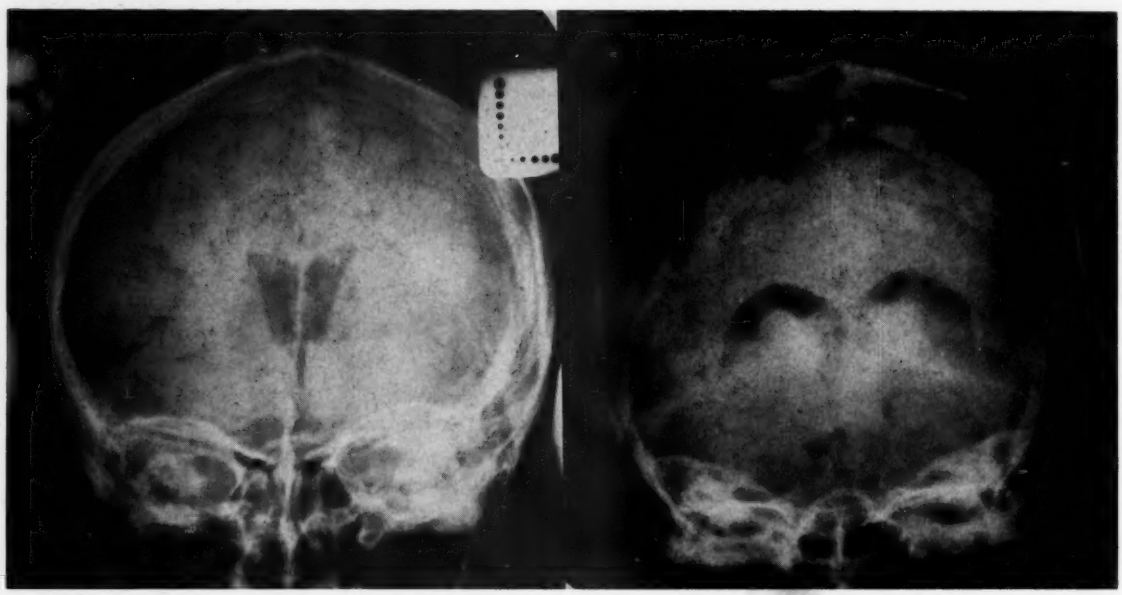

Fig. 8. Case J. Mc., aged fourteen. (Referred by Dr. R. Masland, Salem, N. C.) Focal cerebral seizures from age of nine. Lateral ventricles symmetrical, petrous pyramid and floor of middle fossa higher on the left than on the right. The electroencephalogram showed a "spike" focus in left temporal region. Seizure pattern pointed to deep temporal region. No abnormality in physical or mental examination; righthanded.

Occasionally calcification appears in areas of cortex which are abnormal and epileptogenic as the result of birth ischemia, but this is rare. Calcification may also

[1] Penfield, W., and Ward, A. A., Jr. Calcifying epileptogenic lesions. *Arch. Neurol. & Psychiat.*, 1948, *60*, 20–36.

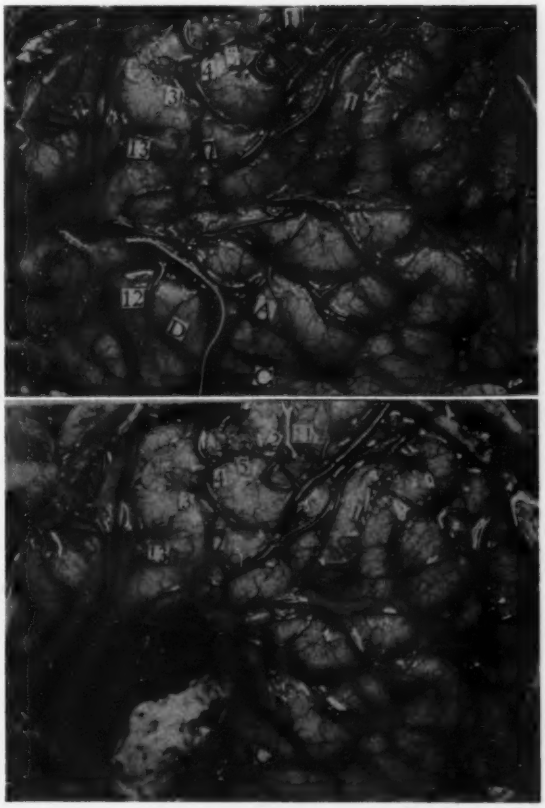

Fig. 9. Case J. Mc. Operative exposure of left sylvian region. There was whitening of the pia-arachnoid. Numbered tickets record positive responses to stimulation. In the upper frame the white thread indicates line of projected excision. In the lower frame the anterior end of the temporal lobe has been excised.

The first temporal convolution, deep in the fissure of Sylvius, was tough and grayish-yellow in color. This abnormality extended on into the uncus and hippocampus. Cause obviously birth ischemia. The excision of the anterior 5 cm. of temporal lobe included the uncus and hippocampus.

Aphasia appeared on second postoperative day and disappeared completely before leaving hospital.

take place in certain poorly understood degenerative conditions of the brain.

### G. BONE PLAQUES

Flat bone plaques are encountered in the subdural space. There is usually evidence in these cases of the existence of a subdural hematoma many years earlier. We have encountered three examples of bone formation in the subarachnoid space—clearly beneath the arachnoid and outside the pia mater.

These examples of subdural and subarachnoid bone were encountered in the vicinity of epileptogenic areas of atrophic cortex. But they did not seem to correspond exactly to the location of focus. It seems likely that in each case a blood clot was left behind in the subdural or subarachnoid

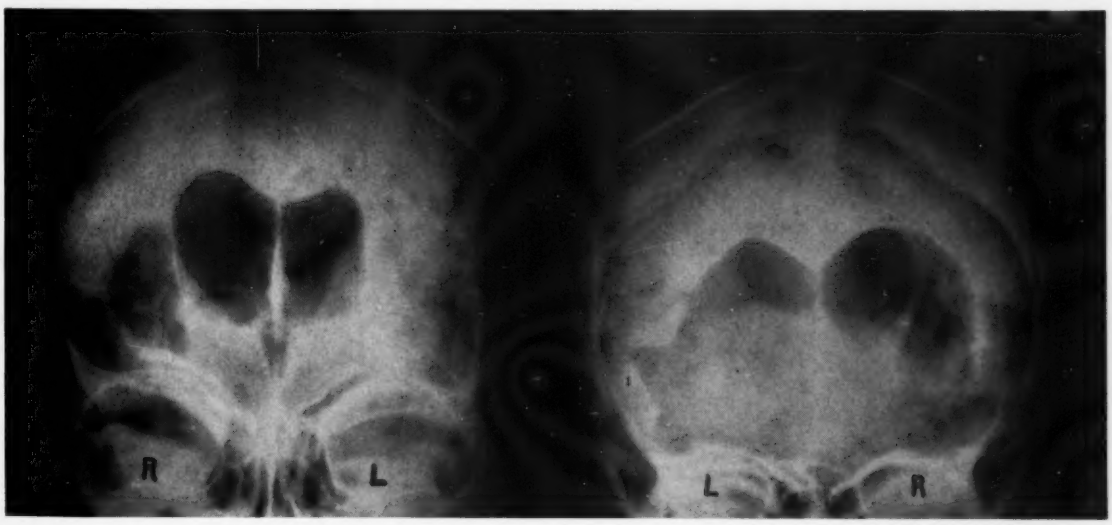


Fig. 10. Case H. M., aged sixty-one. Enlargement of right lateral ventricle and cyst in right hemisphere, resulting from cerebral embolism ten years earlier. There is reflected contralateral enlargement of left lateral ventricle.

space at the time of the traumatic injury to the brain that was the original cause of the seizures.

Bone plaques are also found upon the dural reflections, especially the anterior portion of the falx cerebri (Fig. 11). It is in this area that the falx is often deficient. Holes are present in it as though the membrane had been torn. Not infrequently the surgeon or the pathologist discovers adhesions between the two frontal lobes through these holes.

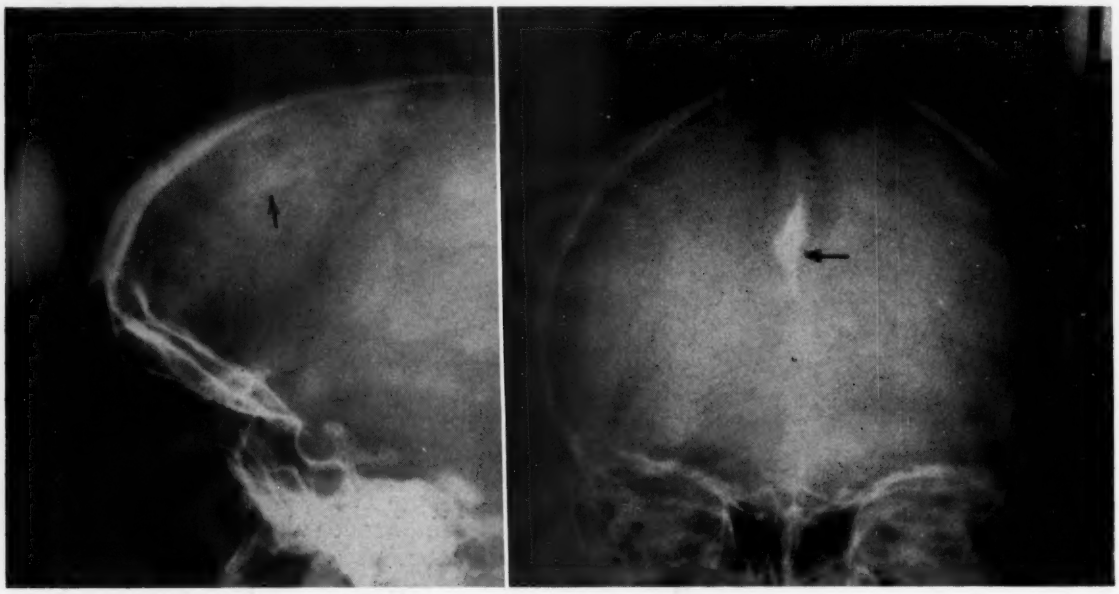

Fig. 11. Case B. L., aged twenty-nine. Symptomless bone plaque situated upon the anterior-superior portion of the falx cerebri.

The probable cause is not difficult to surmise. During the moulding of the infant's head as it passes through the birth canal, tears of the falx are not at all rare. It has frequently been pointed out that tears, near the entrance of the great vein of Galen into the straight sinus, are associated with subdural bleeding.

Tears of the falx anteriorly are probably still more frequent, but as they lead to no immediate symptoms they have been ignored. Scars of the falx in this area occasionally give rise to chronic headache.[2]

[2] Penfield, W., and McNaughton, F. Dural headache and innervation of dura mater. *Arch. Neurol. & Psychiat.*, 1940, *44*, 43–75.

### H. CRANIAL RESPONSE TO TUMOR AND CYST

A superficial tumor of the brain, if present for a sufficiently long time, gives rise to thinning of the overlying cranium. This is too well recognized to require illustration.

A fluid filled cyst on the surface of the brain may produce the same effect in time if it is a cyst that does not communicate with the ventricle.

Meningeal fibroblastomas (meningiomas) sometimes affect the bone in a very different way. Instead of eroding the inner table of the skull, the cells of this neoplasm enter the haversian canals of the overlying bone and produce new bone formation. This results in an exostosis and sometimes also an enostosis. The neoplasm may thus pass through the bone into the periosteum and overlying muscle.

### I. CRANIOCEREBRAL EROSIONS

When there is a deficiency in the dura, the brain has an extraordinary effect upon the under side of the cranium. It erodes it in an uneven "pebbly" manner. This is true even when brain is covered by intact

pia-arachnoid, as shown in Case N. S., Figures 12 and 13. In Figure 13 it may be seen that the dura, which must have been torn away from under the bone, has left the arachnoid of the brain intact.

We have encountered many cases in which the dura has been left open beneath intact bone at the time of a previous craniotomy. This results in the rapid appearance of irregular bone erosion even in the absence of increased intracranial pressure. This is seen in Figure 14 where dura had been removed four years earlier.

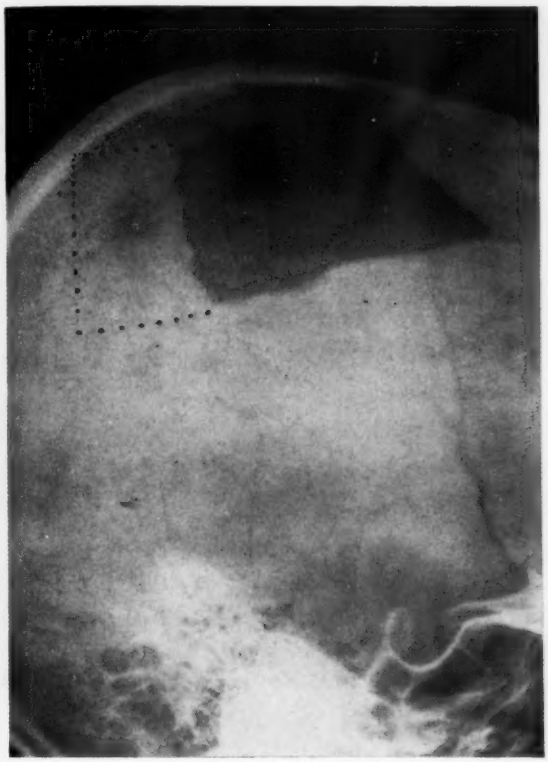

Fig. 12. Case N. S., aged twenty-eight. (Referred by Dr. H. L. Scamell, Halifax.) Head injury and operative removal of bone fragments at the age of twenty-two. Bone erosion due to absence of dura seen on the left of the cranial defect.

Deficiency in the dura is produced frequently by a wide fracture of the skull or a depressed fracture. The dura seems to be torn by the original impact. It may be pulled away, or left in shreds in the vicinity of the fracture. This produces a zone of bone erosion adjacent to the crack. This is illustrated in Figure 15.

Fig. 13. Case N. S. A small bone flap has been turned at the edge of the cranial defect, as indicated by dotted line in Figure 12. Erosion of undersurface of bone due to direct contact of brain covered by intact arachnoid membrane. The dura must have been torn away at the time of the depressed fracture six years earlier.

Depressed fracture of the skull may leave lacerated brain in contact with the undersurface of the skull, as shown in Figures 16 and 17. In the latter figure erosion is shown alternating with little islands of bone thickening.

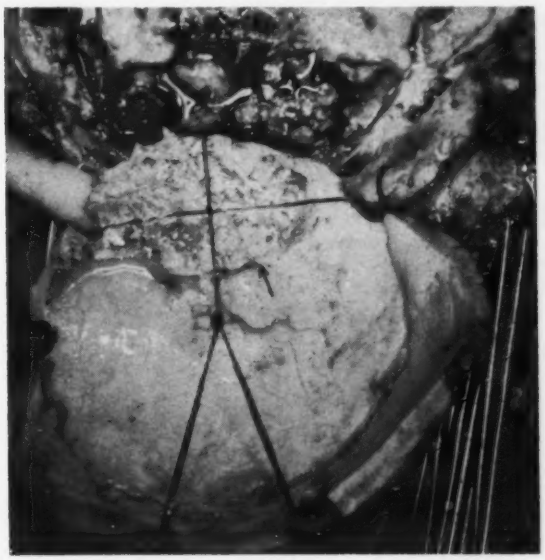

Fig. 14. Case E. M., aged twenty-eight. (Referred by Dr. Sam Dunn, Lubbock, Texas.) Craniocerebral erosion due to operative removal of dura over intact brain four years earlier. The outline of the previous bone flap may be seen and the bone erosion corresponding to the excised dura.

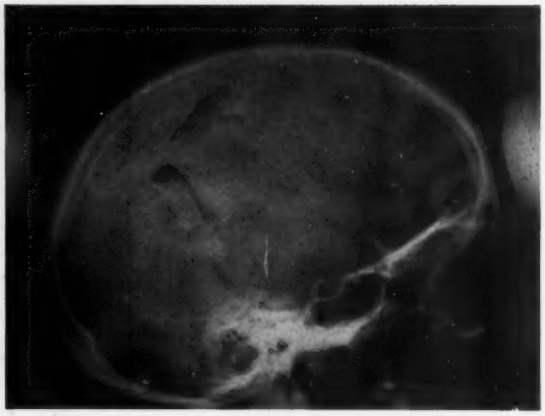

Fig. 15. Case C. Mc., aged thirty. (Referred by Dr. C. M. Morrison, New Waterford, Cape Breton, N. S.). Fracture of skull, erosion of bone. Fracture of skull occurred at the age of eight. Focal cerebral seizures began at the age of thirteen. When a parietal bone flap was turned, the underlying dura was found to be deficient in areas corresponding with the bone erosion.

We have called the effect of brain against bone craniocerebral erosion. It is not smooth. On the contrary, as the foregoing illustrations show, it is very irregular. Small stalactites may be found in the bed of the eroded area. There may also be smooth bone thickening on the border of such erosions, as in Case P. R. (Fig. 16 and 17).

It seems likely that when there is increased intracranial pressure, this erosion takes place more rapidly, for I have seen the thickness of cranium eroded to half its preoperative width in a seven month period, when increased pressure was present as well as dural defect.

The only satisfactory substitute for dura is the transplantation of more dura or of some living dura-like membrane, such as periosteum or fascia. One of the worst substitutes is preserved animal membrane.

The metallic sheets and plastic sheets are not as objectionable as they allow connective tissue to form and thus produce a dura-like membrane on both sides. But these foreign substances do not serve any useful therapeutic purpose.

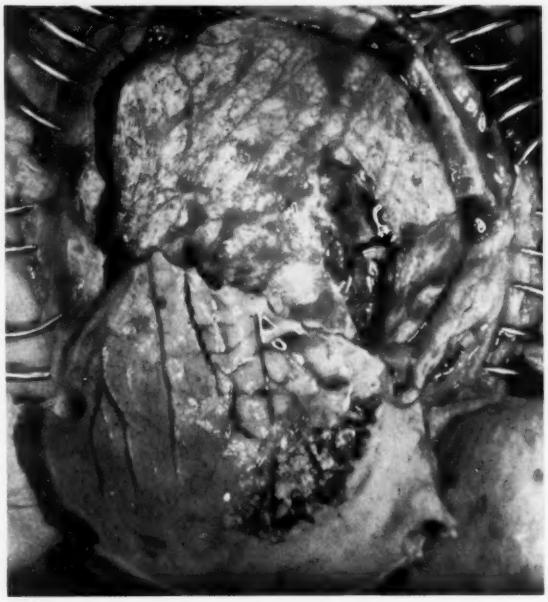

Fig. 17. Case P. R. Craniotomy. The bone flap has been turned down showing dural defect. Cranial erosion corresponds to the dural defect. The margins of the dura were found to be turned into the brain at the edges of the defect. Pneumograms showed the ventricles to be little altered in size. Radical excision was carried out.

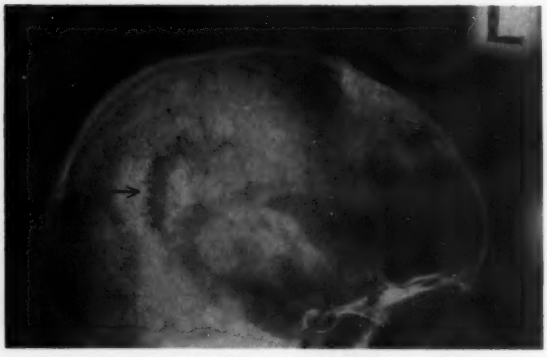

Fig. 16. Case P. R. aged nineteen. (Referred by Dr. Sylvio Caron, Quebec.) Craniocerebral erosion. This boy had a skull fracture at fourteen months of age, probably depressed. Focal cerebral seizures began at the age of seventeen.

When a surgeon carries out a craniotomy in the hope of relieving a patient of focal cerebral seizures, he must excise the epileptogenic area cleanly, leaving the best degree of circulation possible in the banks of excision. If this cannot be done, it is better to leave the brain alone. The removal of adhesions and the interposition of other

substances to replace the dura is useless, sometimes worse than useless. Subtemporal decompression is a waste of time, and dural removal as a therapeutic measure is ill considered folly.

Curiously enough, it is difficult to prove that dural absence in itself has any undesirable effect upon the brain. It has not been our experience that such areas form foci for the production of epileptic seizures. In Case P. R. (Fig. 16 and 17) it did correspond with the epileptogenic focus but usually it has been in the neighborhood of such foci.

We have applied the term *craniocerebral erosion* to the effect of brain upon bone but it is not altogether clear whether or not the brain which has lost its leptomeningeal covering will cause this erosion. Certainly when nothing but arachnoid and pia separate the bone from brain, this erosion does take place.

A familiar example of effect of arachnoid on bone may be cited. Under normal conditions, arachnoidal thickenings form at various points in the vicinity of dural sinuses. These thickenings, or granulations, penetrate the dura and seem to provide for more ready passage of cerebrospinal fluid from subarachnoid space to venous lakes.

However, the arachnoid granulation often passes through the dura so that it presents itself as a little knob, like a vegetation, on the outside of the dura. These bodies, which were described by Antonio Pacchioni many years ago, and the depressions which they form in the skull are familiar to all radiologists (see Fig 18).

I can seen no reason why the pacchionian granulation should exert a greater pressure upon the bone than is exerted upon it elsewhere by the cranial contents through the dura. It seems likely, therefore, that the arachnoidal cells of the granulation erode the bone in the pacchionian depression by the same biological process that causes the arachnoid that covers the brain to erode the undersurface of the cranium when the normally intervening dura is removed or is torn to shreds by trauma.

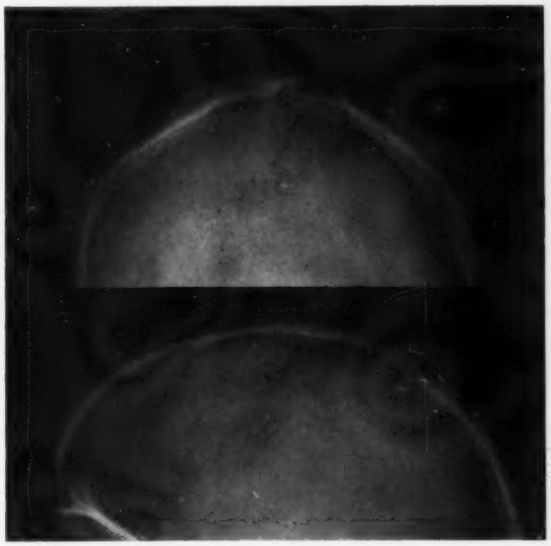

Fig. 18. Case J. P. Normal pacchionian impressions on either side of vertex of skull. The erosion of the undersurface of the bone is produced by contact with arachnoidal granulations.

### J. EPILOGUE

With your permission, Mr. President, I shall conclude these rambling remarks on the human cranium by an epilogue.

Two years ago, while standing in a pit that formed part of the abandoned excavations of the city of Ur, I saw a rounded object protruding from the dry dirt at my feet. Thinking it was just another fragment of a broken urn, I picked it up and dusted it off. But this fragment had a curious green color and its edges were serrated in the form of the sutures of the skull. I turned it over and inspected its concave interior.

I felt a chill run down my spine. No potter's wheel had shaped this urn. It was the occipital bone of a man, so dry and brittle that a piece broke off in my hand. The clay vessels which had been uncovered in this pit must have contained water, wine and milk four to five thousand years ago.

What about the man whose skull this was? I studied the bone carefully. A well formed external occipital protuberance bore testimony to the strength of his neck muscles. The imprint of the convolutions of his occipital lobes was plainly seen on the inner table and the pressure of blood that flowed

through the sinuses had also left a patterned impression.

Surely the brain that once throbbed within this skull must have been normal, and the man? . . . . perhaps a proud citizen of Ur, the capital of Sumer. It was here, on the banks of the Euphrates River, that the Sumerians had created the art of writing and reading and the system of laws that was to reappear in the code of Hammurabi and in the Ten Commandments.

In retrospect their contributions to posterity seem to rank with our own—and yet their civilization vanished, and Ur was lost to sight and to memory under the drifting dust of the desert. War's madness brought their downfall.

It may yet be, in some future age, when the fever of our own madness is past, when atomic wars have come and gone, . . . . it may be, I say, that we shall have been forgotten.

Then perhaps some wise physician of a gentler race will find a lonely beach where waves wash up the skulls of this generation like empty shells from the sea.

I wonder if he will stoop and pick them up and read in them the story of our lives. I wonder if the cranial clues we have discussed may help him to undertand our misfortunes, even though he cannot guess the dreams that would forever haunt that shore.

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Vol. 67, No. 4

# FORAMINA PARIETALIA PERMAGNA

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UNUSUALLY large parietal foramina have been investigated with great thoroughness by Greig (1927), who considers that the condition is "sufficiently rare to make it desirable that every example be reported."

The human parietal foramen (foramen parietale), present in some 60 per cent of cases, is more commonly unilateral than bilateral; rarely it is multiple, or accompanied by or replaced by a single median (sagittal) foramen (Boyd, 1930). Among Primates, it is absent in the Lemuroidea, rare in monkeys, and occasionally present in the Anthropomorpha, especially the gorilla (Boyd, 1934). The human parietal foramen transmits an emissary vein (v. emissaria parietalis, B.R.; Emissarium, B.N.A.; Santorini's* vein) which connects the occipital veins with the superior sagittal sinus, and also a minute anastomosis between the middle meningeal and occipital arteries (R. meningeus A. occipitalis).

More than 90 per cent of parietal foramina do not exceed 1 mm. in diameter. The remainder vary in size up to some 50 mm. Such unusually large openings (foramina parietalia permagna, Pamperl, 1919; fenestrae parietales symmetricae, Zarfl, 1936†) form a well defined clinico-anatomical entity, but precise definition of what constitutes an unusually large foramen is precluded by the existence of a graduated series of medium-sized foramina. In 1,500 skulls in the University of Edinburgh Anatomical Museum Boyd (1930) found only one instance which he considered "abnormally large"; Moore (1949) found no example in 1,500 skulls in the Terry Osteological Museum, Washington University School of Medicine. Greig (1927) states that the condition is more frequent in males than in females in the proportion of 10 to 6. According to Halbertsma (1940) the defect on the right is often larger than that on the left. Cave (1928) maintains that "when one foramen is unduly enlarged, that is the only foramen present"; Derry's (1914) case, however, presented a minute left foramen, in addition to the large right one. The condition occurs in all races (Travers and Wormley, 1938). The first written account of this anomaly was given by Lancisi in Rome, 1707 (Cave, 1928), but the first adequate description was by Turner (1865); the first example in a living person was described by Greig (1892). In addition to his own case, Stallworthy (1932) found 46 instances recorded in the literature, and a considerable number of cases have been published since that date (*e.g.*, Ribadeau-Dumas and Le Melletier, 1935; Weber and Schwarz, 1935; Zarfl, 1936; Pepper and Pendergrass, 1936; Irvine and Taylor, 1936; Alley, 1936; Ellis, 1938; Schaeffer, 1938; Travers and Wormley, 1938; Pendergrass and Pepper, 1939; Halbertsma, 1939 and 1940; Warkany and Weaver, 1940; Goldsmith, 1941 and 1945; Ritvo, 1949; etc.‡), frequently in journals not readily available. Furthermore, it would appear that a number of cases (including Goldsmith's [1922] 16 cases [referred to later] and 4 cases described by Neurath [cited by Zarfl], and several others) were not in-

* G. Santorini (1681–1737).

† We deprecate strongly the use of the term "Catlin mark" (Goldsmith, 1922), which we consider to be a perfect example of futile eponymous terminology; such a meaningless phrase (together with the even more absurd one "eyes in the skull," used by the same writer in a scientific journal, 1941) should not be perpetuated by other authors, as has unfortunately been the case.

‡ No attempt is made here to list all cases recorded and further references to cases will be found in a number of the papers cited.

cluded in Stallworthy's figures. It is likely that cases are seen more frequently now, particularly in vivo, with the increasing use of roentgenography; Moore (1949), however, failed to find the condition in well over 15,000 skull roentgenograms, and he stresses its rarity in several large American museums.

Five new cases are recorded below.

## REPORT OF CASES

Case 1. Man, aged seventy-five. Certified cause of death: senility. No external evidence of the underlying defect was noticed post-mortem. The brain displaced 1,435 ml. of water, and appeared normal. The cranial index, estimated roentgenographically, is 76.5, and the skull is therefore mesocranial (Martin's mesokephal). The calvarium varies from 6 to 11 mm. in thickness and is particularly heavy (442 gm. or 0.9 lb.); a ground section of the left parietal showed the outer table and diploe each 3 mm. in width, and the inner table 1 mm., in the region sectioned. The left side of the vault shows slight flattening, and two large parietal foramina are present (Fig. 1 and 2). A few small ivory exostoses are scattered over both parietal bones and the region around the foramina is hyperostosed. The coronal suture is visible externally throughout its length, but the sagittal suture becomes obliterated for a distance of 56.5 mm. in front of the lambda (*i.e.*, in its pars obelica and pars lambdica). There is no metopic suture. The maximum measurements of the parietal foramina are:

| | | |
|---|---|---|
| Right foramen | Coronal diameter | 11.5 mm. |
| | Sagittal diameter | 9 mm. |
| Left foramen | Coronal diameter | 8 mm. |
| | Sagittal diameter | 8 mm. |

The two foramina are connected by a transverse suture (7.5 mm. in length and with a short vertical extension downwards) 33 mm. in front of the lambda and 23.5 mm. behind the termination of the sagittal suture. In the region of the foramina the bone shows obvious bevelling externally. Figure 3 shows a roentgenogram of the skull cap.

The sagittal sulcus, near the obelion, deviates to the right and is interrupted by the right parietal foramen. A number of meningeal grooves converge on the foramina. The peri-

Fig. 1. External aspect of parietal bones in Case 1. The termination of the pars verticis of the sagittal suture can be seen at the top of the illustration, and the tip of the lambdoid suture is visible at the bottom.

Fig. 2. Internal aspect of parietal bones in Case 1. Note vascular grooves. Figures 1 and 2 are photographs on Kodak Microfile Regular Film taken with a Zeiss Contax II, Sonnar *f*2 (by R. O'R.).

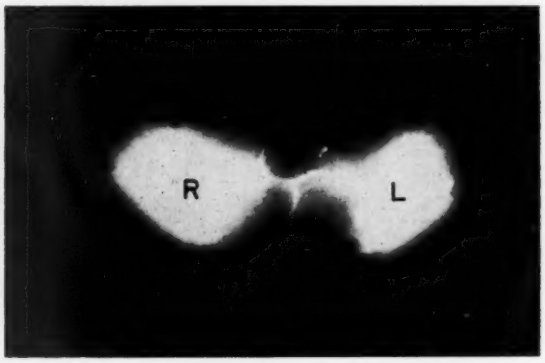


Fig. 3. Roentgenogram of parietal foramina in Case 1. Note the transverse interforaminal suture. In this and in the subsequent frontal roentgenograms the top of the illustration is superior and the right foramen is on the reader's left.

Fig. 4. Roentgenogram of cranial vault in Case II.

cranium and endocranium were continuous around the foraminal margins, and the openings were filled in with connective tissue, through which passed on the right side a vein 2 mm. in diameter connected with the superior sagittal sinus. This sinus communicated with both transverse sinuses. The straight sinus was partitioned by a median septum.

Case II. Boy, aged six in 1942.

1942: Complained of attacks of frontal headache and vomiting, lasting about three days and recurring about every six weeks. Becoming more severe. No visual aura. No fits. Nothing significant in past history. Mother noticed "soft place" at back of head since infancy. Child does well at school. On examination, two soft areas in parietal region were palpable, and a convergent, non-paralytic strabismus was present. Central nervous system normal.

On roentgenography (Fig. 4 and 5), two bony defects about 35 mm. in coronal diameter were present in the region of the parietal foramina and were connected by a transverse suture, from the right side of which extended another and smaller defect. On each side, an accessory suture connected the corresponding foramen with the lambdoid suture at a point about 50 mm. from the lambda; there was no sign of a continuation of these additional sutures forwards anterior to the foramina.

1950: Headaches and vomiting less frequent but occur especially after travelling. On examination, foramina still palpable; general health good.

Another roentgenogram (Fig. 6) showed little change in the appearance and size of the foramina.

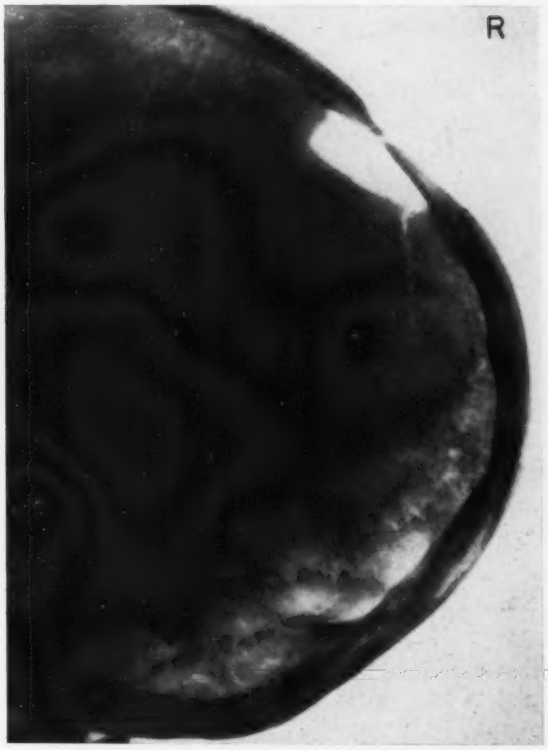


Fig. 5. Right lateral roentgenogram of occiput in Case II. Note the accessory suture extending vertically between the parietal foramen and the lambdoid suture.

Case III. Half-brother of Case II, aged four in 1942. No symptoms. Roentgenogram (Fig. 7) showed two foramina similar in size and

Fig. 6. Roentgenogram of cranial vault in Case II, taken eight years later than Figure 4. Little change in appearance.

Fig. 7. Roentgenogram of cranial vault in Case III (half-brother of Case II).

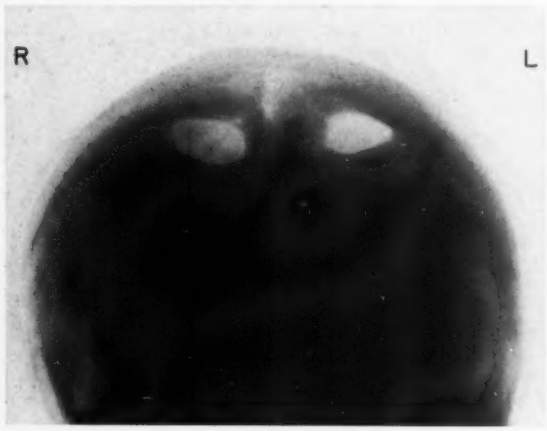


Fig. 8. Roentgenogram of cranial vault in Case IV (mother of Cases II and III).

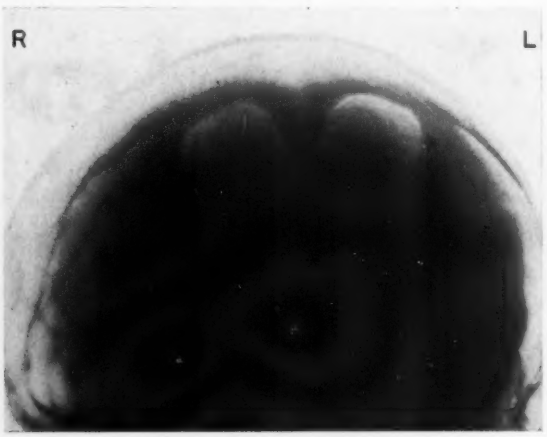


Fig. 9. Roentgenogram of cranial vault in Case V. The foramina are considerably larger in this instance.

appearance to those of Case II, and similar additional sutures were present. There was a suggestion of a small sutural bone between the foramina. Another roentgenogram in 1950 revealed no change.

Case IV. Mother of Cases II and III, aged forty-one in 1942. Has two palpable parietal defects, and states that her father is similarly affected. She has been married twice and of her seven living children she is aware of the defect in only the two previously described half-brothers. She states that moderate pressure on the affected region is painful. Roentgenogram (Fig. 8) showed bilateral foramina each about 20 mm. in coronal diameter. The additional sutures referred to above were not seen. Another roentgenogram in 1950 showed no change.

Case V. Boy, aged five and one-half in 1943. Only child, no symptoms, bright at school. Roentgenogram (Fig. 9) showed two circular foramina, each about 30 mm. in diameter and connected by a transverse suture.

## Development of Parietal Bone

The parietal bone ossifies in membrane from one or two centers in the region of the future parietal eminence at about the seventh or eighth week of intrauterine life (Hill, 1939, classifies the parietals as beginning to ossify at five lunar months, average crown-rump length 194 mm.). Three or four centers have been suggested but have not met with acceptance. Toldt, Ranke, and some other authors (*e.g.*, Noback, 1944) favor bi-ossific development. Patten (1912), however, considered that Ranke's case of two large centers in a third month fetus* was abnormal and that the significance of the term "center" as described by Toldt and other writers is far from clear. He suggested that thickenings in the meshwork formed by a single ossific nucleus have been referred to as separate centers. Mall (1906) described a reticular nucleus at the fifty-sixth day, and a few days later it "is now hour-glass shaped" and "may represent the two centers described by Toldt." More recently, Poirier and Charpy (1931) refer to "un double centre," and Frazer

* Thoma (1913) gives an illustration (Fig. 6 of his paper) of two large centers at 78 mm.

(1940) favored two nuclei but "sometimes apparently only a single centre, though this may be only an instance of very early union." The two nuclei are said to be generally superior (medial) and inferior (lateral), or posterosuperior and anteroinferior.

Extreme caution is necessary in interpreting the number of centers. Apart from the tendency to individual variations in the development of membrane bones, errors concerning the frontal bone were prevalent for many years (Inman and Saunders, 1937) and the falsification of the ontogeny of the mandible is well known (Wood Jones, 1948).

A network of fine trabeculae spreads from the region of the eminence in the form of radiating bony spicules.* In the area of the parietal foramina, the spread of ossification towards the median plane is slower than elsewhere, and "for some time a membranous interval is left, named the sagittal fontanelle.† The fontanelle is lozenge shaped, and the parietal emissary vessels pass through its lateral angles; closure is effected by extension and fusion of the anterior and posterior borders, the parietal foramina being left as remains of the fontanelle" (Quain, 1915).

The sagittal fontanelle (fontanelle obélique, Gerdy's‡ fontanelle) was observed by Augier in 23 out of 45 newborn skulls (Poirier and Charpy). Paterson and Lovegrove (1900), in an examination of 85 parietal bones of ninth month fetuses, found in 70 specimens a cleft in the upper border of the bone in the position of the parietal foramen, with a rounded or oval vascular notch in the lateral angle of the cleft, and Le Double (1903) refers to an incisure parietale in 1 out of 3 newborns. According to Greig (1927) "Broca, as Welcker had done before him, pointed out that the [parietal] foramina were not distinguishable in the new-born." Other writers state that the cleft usually closes in utero, *e.g.*, about the fifth month of intrauterine life (Morris, 1942), and "according to Dr. A. W. W. Lea, a well-developed sagittal fontanelle is present in 4.4 per cent of infants at birth. In such cases it closes within the first two months of life, but at times it may remain open for at least eight months after birth and possibly longer" (Morris).

In the course of obliteration of the sagittal fontanelle a cruciform suture occurs as ossification extends from the four margins of the fontanelle. Usually the vertical limb persists as the pars obelica of the sagittal suture, and the transverse limb becomes obliterated, although it has been found in young children (Poirier and Charpy, 1931). By contrast, in many cases of large parietal foramina (*e.g.*, Cases I, II, III and V of this paper), the transverse limb persists as an interforaminal suture, and the pars obelica becomes obliterated. All four limbs of the cruciform suture can be seen in an illustration by Zarfl (1936). A failure of the spread of ossification at the margins of the fontanelle would result in a persistent sagittal foramen, which has been found by Boyd (1930) in 5.9 per cent of 1,500 crania. Sagittal hemifontanelle has also been recorded (Le Double, 1903). Zarfl (1936) illustrates a sagittal foramen measuring 5.5 by 4 cm. Isolated ossification in the membrane of the fontanelle would result in an "osselet obélique," which has been seen in 0.8 per cent of 500 skulls (figures quoted by Poirier and Charpy); there is a suggestion of this occurrence in the roentgenogram of our third case (Fig. 7).

Some of Goldsmith's (1922) patients claimed that their foramina permagna commenced as one large opening which became divided later. This method of formation has been shown to occur by several writers, and is well exemplified in an excellent series of roentgenograms by Pendergrass and Pepper (1939). Not all cases are formed

* The characteristic radiating trabecular arrangement is traceable to meridional tensions, although the development of bone per se and the site of the ossification centers are not determined by mechanical conditions resulting from direct pressure of the brain; indeed "not many conclusions relating to the mechanics of development in the skull can be accepted as definitely established" (Murray, 1936).

† Some writers confine the term "fontanelle" to regions where at least three bones meet.

‡ P. N. Gerdy (1797–1856).

in the same manner, however, and Halbertsma (1939 and 1940) observed an unusual triradiate spread of ossification in a child. According to Goldsmith (1922), a large parietal foramen "grows smaller, and in some cases closes entirely with age," and Irvine and Taylor (1936) also refer to progressive decrease in size; we have already pointed out that in our Cases II, III and IV we were unable to detect any difference in size after a period of eight years. Broca maintained that normal-sized parietal foramina were relatively larger in persons past middle life and attributed this to amplification of the emissary veins (Greig, 1927); according to Poirier and Charpy (1920) the parietal emissary vein is relatively larger in children than in adults. In a case of localized bony absorption in a child's skull following a fall, a defect of about 1 inch diameter in the frontal bone gradually filled in during a period of nine months (Nicholas *et al.*, 1948); in another case of traumatism a permanent hiatus in the right parietal bone was left (Kellock, cited by Greig, 1927).

The influence of the transmitted blood vessels on the appearance of the parietal foramina appears to be slight. Le Double found complete absence of all vessels in both foramina of an eight year old child (Poirier and Charpy, 1931). There is no evidence that an enlarged foramen transmits a large vein (Boyd, 1930), as is borne out by our postmortem case.

So far, we have assumed with Pendergrass and Pepper (1939) that foramina permagna arise merely as a delay in an otherwise normal ossific process. Some writers, however, *e.g.*, Zarfl (1936) and Halbertsma (1939 and 1940), consider that the large foramina are not "identical with the normal anatomical parietal foramina." We interpret this to mean that the two types do not show interindividual (Owen's "special") "homology" in the sense of possessing an "essential structural similarity" (Boyden, 1947). Ontogenetic development would seem to be the sole criterion available here (see Szarski, 1949) and Goldsmith (1941) considers that the large openings may be "superimposed" on the normal foramina. We know of no evidence in favor of independent genetical determination (Gates, 1946). We do not consider that present knowledge of the development of parietal foramina in general is adequate to pass judgment on the above issues.

"Homology" based on similarity in adult structural organization is of little help here. Goldsmith (1941) cites Sosman's cases in which normal foramina occurred together with large openings.* We would point out, however, that multiple normal-sized foramina occur also (and are more frequent than large foramina); in Boyd's series of 1,500 skulls the parietal foramina were multiple on one or both sides in 2.5 per cent of cases (whereas only one abnormally large foramen was found). Furthermore, the occurrence of additional foramina may perhaps be favored by the presence of delayed ossification in the region, particularly in association with the multiplicity of transmitted vessels (passing through a cribriform membrane) which has been described in some specimens (Greig, 1927, p. 644).

Halbertsma (1939 and 1940) prefers Zarfl's term "fenestrae parietales symmetricae" to Pamperl's name "foramina parietalia permagna" as he considers it more in accord with the viewpoint expressed above. Even if the non-homologous concept should prevail, however, we find little objection to the purely descriptive term "foramina parietalia permagna."†

## PARIETALE BIPARTITUM AND SUTURAL BONES

Owing to the presence of additional sutures in our cases we include a discussion relating to their formation.

* This appears to have been the case in other instances too, *e.g.*, Symmers, 1895. From the irregular borders in our Case 1 (Fig. 1 and 2) the possible formation of additional small foramina can easily be visualized, and in some recorded cases offshoots from the foraminal margins have been noted (*e.g.*, Greig, 1927, Fig. 3).

† "Foramina parietalia permagna" need not imply interindividual homology with "foramina parietalia" any more than does "foramen ischiadicum majus" with "foramen ischiadicum minus."

The nomenclature of accessory bones in the parieto-occipital region is exceedingly obscure and it is very difficult to compare such terms as inca bone, interparietal, preinterparietal, os transversum, os quadratum, triquetrum, os apicis squamae occipitalis, triangulare, tricuspidale, lambdatique, épactal, Goethe's bone. With the exception of the interparietal, Wood Jones dismisses all such names, and states that accessory ossicles in this region should be called lambdoid ossa suturaria (Buchanan, 1949). The preinterparietal will be discussed later.

The term interparietal is used when the superior part of the squamous occipital, which is developed in membrane, persists as a separate bone; it is limited below by the sutura mendosa (suture biastérique). The bone is sometimes called os incae, but its incidence is higher in some groups other than Peruvian (Sullivan, cited by Hoheisel, 1930). In our Cases II and III the lambda appears to occupy its usual site and we therefore consider that the area of bone bounded by the accessory, interforaminal, and lambdoid sutures is not an interparietal bone. The accessory suture commences in the region of the "incisure paralambdatique," where a sutural bone is often found (Poirier and Charpy, 1931). Somewhat similar sutures were present in 2 cases described by Maciesza (1910), but in a number of recorded cases it is difficult to determine the precise topography of the bones; thus, we find difficulty in correlating Greig's (1927) Figure 7 with his description of the specimen.

Os parietale bipartitum has been described in many Primate skulls (Patten, 1912; Peters, 1932). It has been seen in the fetus and in infants as well as in adults, and is commoner in males. The bone may be multipartite. The division (subsagittal, parietal, or intraparietal suture) may run in almost any direction and may be partial or complete.*

Patten attributed the multipartition of the parietal in a chimpanzee to divisions of one center: "there was originally a single center which thickened in two parts, the upper undergoing further thickenings of its ossific deposits to form multiple nuclei" (p. 562), but he also allowed that "under certain conditions of bone development, multipartite segments of the parietal bones can originate from primary ossific centers, *i.e.*, centers whose appearance is cotemporary with the appearance of the main centers or center of ossification" (p. 554).

Poirier and Charpy (1931) describe similar methods of development of accessory bones but refer to the resultant ossicles as "os wormiens" (p. 612). Patten (1912), however, confined the term "Wormian† bones" to those "whose centers begin to appear when the primary centers have done their work" and which "have a definite office to fulfill, namely to form ossified plates which supplant the membranous gaps in the vault left after the primary center or centers had exhausted their powers to spread their ossific material sufficiently far as to allow of only a sutural or an intersutural breach in the continuity of the cranial vault appearing" (pp. 561–562). Frazer's (1940) definition (p. 191) is similar, but later in his book he refers to "false" sutural bones (p. 274) in a manner which we do not find clear. Hess (1946) suggests a compensating function in lateral expansion of the skull. The functional significance of sutural bones is not as simple as outlined above, however, for it has been pointed out (Poirier and Charpy) that these ossicles occur less frequently in the larger fontanelles and sutural spaces, *e.g.*, the anterior fontanelle and the sagittal suture; and it must be kept in mind that sutures are not merely the meeting places of several ossific centers but are "morphologically predetermined before the process of ossification is complete" (Le Gros Clark, 1945), as shown by Troitsky's experiment

* Extra parietal sutures have been observed in some cases of cleidocranial dysostosis (Kilgore and Lasker, 1946).

† O. Worm (1588–1654). Sutural bones "had been observed by earlier anatomists but they were well described by Worm and were called Wormian bones by his nephew, Thomas Bartholin" (Skinner, 1949).

in which, after complete excision of a developing parietal bone, a new ossific center appeared and a normal-sized parietal regenerated, with no tendency of the neighboring bones to invade the area of excision.

Wood Jones (Buchanan, 1949) maintains that sutural bones may reach "several inches in diameter"; such a large size would seem to require development from an early stage. According to Le Gros Clark (1945) sutural bones "are formed by the detachment of ossifying spicules at the margins of the growing bones," and a similar mode of origin is given in Quain (1915). Hess (1946) divides ossicula wormiana into those which "represent originally independent abnormal bones" and those which are "the product of nuclei detached from the main regular osteogenic centers," appearing later, perhaps postpartum. The same author states that Wormian bones are characterized by a straight or delicately serrated suture line and that the majority are preformed in membranes. It is clear that there is no agreement concerning the developmental distinction between bipartite and "Wormian" bones, and that accessory cranial ossicles may ossify (a) either very early in intrauterine life, or at a late period, perhaps postnatally; and (b) either by fragmentation of a primary ossific center, or from an independent nucleus. Sutural bones are a characteristic feature of cleidocranial dysostosis, and occur also with other cranial defects, *e.g.*, hypertelorism, and with congenital anomalies of the nervous system. Hess (1946) considers that these skeletal abnormalities are related to "a metabolic disorder of the mesoderm" and he classifies them under the heading "hypostosis."

Two "preinterparietal" centers have been figured in a 75 mm. embryo by Poirier and Charpy (1931, p. 160), who state that a persistent preinterparietal bone was found partially or completely free in 4 per cent of 669 skulls by Stieda. These authors maintain that the two preinterparietal centers may unite to form a median bone, or less frequently persist as two, or may appear unilateral. Union with the squamous occipital may advance the apex of the apparent parieto-occipital articulation cephalad between the parietals; this appearance is called "apophyse linguiforme du lambda" by Le Double (1903). Such centers in an embryo, were they to remain separate, would lead to a condition indistinguishable from that of bipartite parietal as described by Patten. Sutures ("sutures angulaires") have been found separating one angle of the parietal bone, *e.g.*, the posterosuperior angle, forming in this case the "os lambdatique." This bone is listed by Poirier and Charpy (1931) under the heading "Pluripartition du pariétal" (p. 315) and also under the title "Os wormiens" (p. 611). In more than 200 fetuses under eight months no example of the os lambdatique was encountered (p. 612).

## DISCUSSION

Some of the underlying factors in the production of foramina parietalia permagna can be discussed independently of the problems of homology between large and normal-sized foramina referred to earlier. In the recorded cases various authors have listed metopism (*e.g.*, Stallworthy, 1932), microcephaly, synostosis of sutures, and plagiocephaly (*e.g.*, Stibbe, 1929), and thinness of the parietal bones (Boyd, 1930; regarding thinness see also Wilson, 1947; Camp and Nash, 1944; Cave, 1927; and Greig, 1926) as conditions associated with large parietal foramina. According to Pancoast *et al.* (1940) thinned areas sometimes give way, causing a unilateral or bilateral defect, and Moore (1949) believes that large foramina are an example of symmetrical thinning of the parietal. There appears to be a difference of opinion as to the incidence of anomalies, cranial or in other regions, associated with foramina parietalia permagna. Warkany and Weaver (1940), who favor a high incidence, give a valuable review of associated developmental abnormalities which have been recorded in various published cases. Metopism, microcepahly, and parietal thinning were not

present in our series, but Case I was plagiocephalic and showed synostosis of the pars obelica and pars lambdica of the sagittal suture; this last is a usual finding in such cases but in a few instances the sagittal suture was complete (*e.g.*, Greig, 1927, Fig. 3). It is difficult to determine the condition of the sagittal suture in our living cases. We are unaware of any defects in any other regions of the body in our series.

Greig (1927) regards the local cranial affection as a manifestation of a general disturbance: "both the skulls I have described in this paper were microcephalic. The enlargement of the foramina is secondary to the microcephaly and is not a primary peculiarity"; clearly a view dependent on microcephaly is not applicable to many instances. Pepper and Pendergrass (1936), by contrast, consider that the "defect is an erratic hereditary anomaly of ossification, bearing no relation to any disease of the skeleton." There appears to be no evidence for Cockayne's contention (cited by Gates, 1946) that the condition is a form of aplasia cutis congenita.

Some observations pertaining to experimental embryology are of interest. Warkany and Schraffenberger (1947) found that roentgen irradiation of pregnant rats was followed by growth retardation of the parietals with defects in the parietal-interparietal region in the fetuses. Barnicot (1950) attached fragments of crystalline vitamin A acetate to pieces of mouse parietal and found that resorption, often leading to perforation of the bone, occurred when the pieces were grown in the cerebral hemisphere of litter mates.

In addition to the hereditary cases described by Pepper and Pendergrass (1936), these writers list seven previous authors who published hereditary series, and a number of such cases have been published since. Alley (1936) shows the condition in twins; the larger twin had very large foramina but her smaller twin brother's foramina appear small from the roentgenogram. It has already been pointed out that Case IV in our series was the mother of Cases II and III. Goldsmith (1922), who traced the affection through five generations and found it in 16 individuals, did not regard it as falling "in line with the usual laws of inheritance" but he considered that his evidence was insufficient for a definite conclusion.

Although foramina parietalia permagna are rare, the possibility of their presence has to be kept in mind in the differential diagnosis of defects of the cranial vault. Conditions to be distinguished are meningocele, meningoencephalocele, dermoid cyst, secondary neoplasm, multiple myeloma, syphilis, xanthomatosis (Hand-Schüller-Christian disease), cleidocranial dysostosis, osteoporosis circumscripta, parietal thinning, craniolacunia, craniofenestria, renal and celiac rickets, trauma, and trephine openings.* The dangers of local injury and/or infection in cases of large parietal foramina are evident.

We are indebted to Dr. T. Lodge, F.F.R., for the roentgenograms, to Prof. E. J. Wayne, F.R.C.P., for permission to publish Cases II–IV and for the 1942 clinical notes thereon, and to Mr. A. W. Fawcett, F.R.C.S., for permission to publish Case V.

## SUMMARY

1. Five cases of large parietal foramina are described and illustrated. One of the cases was found postmortem and the others occurred in vivo.

2. In some of these an additional sagittal-lambdoid suture was found.

3. The development of the parietal bone and its variations is described and correlated with the above anomalies.

4. Three of the cases occurred in one family.

5. Re-examination roentgenographically of these three cases after an interval of eight years revealed little change in size or appearance.

6. The condition is an erratic hereditary

* Prehistoric trephining was usually performed "on the upper and posterior part of the parietal bone," probably because of the easy accessibility of this region to the operator (Moodie, 1923). On the question of trephine openings and large parietal foramina see, for example, Goldsmith (1941 and 1945), Shapiro (1941), and Moore (1949).

anomaly of ossification, sometimes associated with other irregularities of cranial development.

7. Large parietal foramina should be kept in mind in the differential diagnosis of defects of the cranial vault.

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REFERENCES

1. Alley, R. G. Enlarged parietal foramina. *Radiology*, 1936, *27*, 233–235.
2. Augier. See Poirier et Charpy.
3. Barnicot, N. A. Local action of vitamin A on bone. *J. Anat.*, 1950, *84*, 374–387.
4. Boyd, G. I. Emissary foramina of cranium in man and anthropoids. *J. Anat.*, 1930, *65*, 108–121.
5. Boyd, G. I. Emissary foramina of cranium in primates. *J. Anat.*, 1934, *69*, 113–117.
6. Boyden, A. Homology and analogy; critical review of meanings and implications of these concepts in biology. *Am. Midland Nat.*, 1947, *37*, 648–669.
7. Buchanan. Manual of Anatomy. Eighth edition. London, 1949.
7a. Camp, J. D., and Nash, L. A. Developmental thinness of parietal bones. *Radiology*, 1944, *42*, 42–47.
8. Cave, A. J. E. Bilateral and unilateral thinning of parietal bone. *J. Anat.*, 1926–1927, *61*, 486–487.
9. Cave, A. J. E. Two cases of congenitally enlarged parietal foramina. *J. Anat.*, 1928–1929, *63*, 172–174.
10. Clark, W. E. Le G. The Tissues of the Body. Second edition. Oxford University Press, New York, 1945.
11. Derry, D. E. Parietal perforation accompanied with flattening of skull in ancient Egyptian. *J. Anat. & Physiol.*, 1913–1914, *48*, 417–429.
11a. Ellis, R. W. B. Congenital parietal foramina. *Proc. Roy. Soc. Med.*, 1938, *31*, 923.
12. Frazer, J. E. The Anatomy of the Human Skeleton. Fourth edition. J. & A. Churchill, Ltd., London, 1940.
12a. Gates, R. R. Human Genetics. The Macmillan Company, New York, 1946, Vol. I.
13. Goldsmith, W. M. Catlin mark; inheritance of unusual opening in parietal bones. *J. Hered.*, 1922, *13*, 69–71.
14. Goldsmith, W. M. Bilateral fenestrae in parietal bones. *J. Hered.*, 1941, *32*, 301–309.
15. Goldsmith, W. M. Trepanation and "Catlin mark." *Am. Antiquity*, 1945, *10*, 348–352.
16. Greig, D. M. Congenital and symmetrical perforation of both parietal bones. *J. Anat. & Physiol.*, 1891–1892, *26*, 187–191.
17. Greig, D. M. On symmetrical thinness of parietal bones. *Edinburgh M. J.*, 1926, *33*, 645–671.
18. Greig, D. M. Abnormally large foramina parietalia. *Edinburgh M. J.*, 1927, *34*, 629–648.
19. Halbertsma, T. Fenestrae parietalis symmetricae. *Maandschr. v. kindergeneesk.*, 1939, *9*, 89–98.
20. Halbertsma, T. Fenestrae parietales symmetricae. *Arch. Dis. Childhood*, 1940, *15*, 115–120.
21. Hess, L. Ossicula wormiana. *Human Biol.*, 1946, *18*, 61–80.
22. Hill, A. H. Fetal age assessment by centers of ossification. *Am. J. Phys. Anthropol.*, 1939, *24*, 251–272.
23. Hoheisel, W. F. Anomalous Indian occiput. *Anat. Rec.*, 1930, *45*, 129–135.
24. Inman, V. T., and Saunders, J. B. de C. M. Ossification of human frontal bone, with special reference to its presumed pre- and post-frontal elements. *J. Anat.*, 1937, *71*, 383–394.
25. Irvine, E. D., and Taylor, F. W. Hereditary and congenital large parietal foramina. *Brit. J. Radiol.*, 1936, *9*, 456–462.
26. Jones, F. W. Hallmarks of Mankind. Williams & Wilkins Company, Baltimore, 1948.
27. Kilgore, S., and Lasker, G. W. Cleidocranial dysostosis with psychosis. *Arch. Neurol. & Psychiat.*, 1946, *56*, 401–416.
28. Le Double, A.-F. Traité des variations des os du crâne de l'homme et de leur signification au point de vue de l'anthropologie zoologique. Paris, 1903.
29. Macieza, A. Ueber zwei neue Fälle angeborener abnorm weiter Foramina parietalia. *Virchow's Arch. f. path. Anat.*, 1910, *200*, 359–366.
30. Mall, F. P. On ossification centers in human embryos less than one hundred days old. *Am. J. Anat.*, 1905–1906, *5*, 433–458.
31. Moodie, R. L. Paleopathology. Urbana, Ill., 1923.
32. Moore, S. On Catlin mark. *Am. Antiquity*, 1949, *14*, 225–226.
33. Morris, H. Morris' Human Anatomy. Tenth edition. The Blakiston Company, Philadelphia, 1942.
34. Murray, P. D. F. Bones. Cambridge University Press, London, 1936.
35. Nicholas, F. G., Furst, H. C., and Tepper, R. Case of localised traumatic bone absorption in skull. *Brit. J. Radiol.*, 1948, *21*, 67–69.
36. Noback, C. R. Developmental anatomy of human osseous skeleton during embryonic, fetal and circumnatal periods. *Anat. Rec.*, 1944, *88*, 91–125.
37. Pamperl, R. Foramina parietalia permagna. *Deutsche Ztschr. f. Chir.*, 1919, *148*, 91–110.
38. Pancoast, H. K., Pendergrass, E. P., and Schaeffer, J. P. The Head and Neck in

Roentgen Diagnosis. Charles C Thomas, Publisher, Springfield, Ill., 1940.

39. Paterson, A. M., and Lovegrove, F. T. Symmetrical perforations of parietal bones. *J. Anat.*, 1900, *34*, 228–237.
40. Patten, C. J. Cranium of adolescent chimpanzee showing bilateral and symmetrical complete bipartite division of parietals, with multipartite division of upper segments, with remarks on significance of parietal division. *Ztschr. f. Morphol. u. Anthrop.*, 1912, *14*, 527–608.
41. Pendergrass, E. P., and Pepper, O. H. P. Observations on process of ossification in formation of persistent enlarged parietal foramina. Am. J. Roentgenol. & Rad. Therapy, 1939, *41*, 343–346.
42. Pepper, O. H. P., and Pendergrass, E. P. Hereditary occurrence of enlarged parietal foramina. Am. J. Roentgenol. & Rad. Therapy, 1936, *35*, 1–8.
43. Peters, H. B. Über Naht-Anomalien und -Variationen am Primaten-Cranium. *Ztschr. f. Morphol. u. Anthrop.*, 1932, *30*, 317–372.
44. Poirier, P., and Charpy, A. Traité d'anatomie humaine. Third edition. Paris, 1920, Vol. 2, Fasc. 3.
45. Poirier, P., and Charpy, A. Traité d'anatomie humaine. Fourth edition. Paris, 1931, Vol. 1, Fasc. 1, Div. 1.
46. Quain. Elements of Anatomy. Eleventh edition. London, 1915, Vol. 4, Pt. 1.
47. Ribadeau-Dumas, L., and Le Melletier. Lacune congénitale intéressant les deux os pariétaux. *Nourrisson*, 1935, *23*, 359–362.
48. Ritvo, M. Roentgen Diagnosis of Diseases of the Skull. Paul B. Hoeber, Inc., New York, 1949.
49. Schaeffer, J. P. Excessively large parietal foramina and parietal bone deficiencies. *Anat. Rec.*, 1937–1938, *70*. Abstracts of papers, p. 68.
50. Shapiro, H. L. Gene-made trephines versus homemade trephines. *J. Hered.*, 1941, *32*, 434.
51. Skinner, H. A. The Origin of Medical Terms. Williams & Wilkins Company, Baltimore, 1949.
52. Stallworthy, J. A. Case of enlarged parietal foramina associated with metopism and irregular synostosis of coronal suture. *J. Anat.*, 1932, *67*, 168–174.
53. Stibbe, E. P. Skull showing perforations of parietal bone, or enlarged parietal foramina. *J. Anat.*, 1929, *63*, 277–278.
54. Symmers, W. St. C. Skull with enormous parietal foramina. *J. Anat. & Physiol.*, 1894–1895, *29*, 329–330.
55. Szarski, H. Concept of homology in light of comparative anatomy of vertebrates. *Quart. Rev. Biol.*, 1949, *24*, 124–131.
56. Thoma, R. Untersuchungen über das Schädelwachstum und seine Störungen. 2. Das fötale Wachstum. *Virchow's Arch. f. path. Anat.*, 1913, *212*, 1–67.
57. Travers, J. T., and Wormley, L. C. Enlarged parietal foramina. Am. J. Roentgenol. & Rad. Therapy, 1938, *40*, 571–579.
58. Turner, W. On some congenital deformities of human cranium. *Edinburgh M. J.*, 1866, *11*, 133–141.
59. Warkany, J., and Weaver, T. S. Heredofamilial deviations, enlarged parietal foramens combined with obestity, hypogenitalism, microphthalmos and mental retardation. *Am. J. Dis. Child.*, 1940, *60*, 1147–1154.
60. Warkany, J., and Schraffenberger, Elizabeth. Congenital malformations induced in rats by roentgen rays. Am. J. Roentgenol. & Rad. Therapy, 1947, *57*, 455–463.
61. Weber, F. P., and Schwarz, E. Hereditary large parietal foramina. *Proc. Roy. Soc. Med.*, 1935, *29*, 122–125.
62. Wilson, A. K. Thinness of parietal bones. Am. J. Roentgenol. & Rad. Therapy, 1947, *58*, 724–725.
63. Zarfl, M. Fenestrae parietales symmetricae. *Ztschr. f. Kinderh.*, 1936, *57*, 54–66.

# SYMMETRICAL CALCIFICATION IN THE CEREBELLUM

## A REPORT OF TWO CASES

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INTRACRANIAL calcification is frequently encountered in roentgenologic studies of the skull. Calcification in structures such as the pineal gland, petroclinoid ligaments, falx cerebri and glomus of the choroid plexus are ordinarily recognized with ease and usually are considered as variants from the normal, although assumed to be not of pathological significance.

Of considerably greater importance are the calcifications caused by intracranial neoplasm, tuberculoma, abscess, toxoplasmosis, cysticercosis and subdural hematoma. More obscure in origin, but perhaps related to genetic defects, are such entities as multiple subcortical calcification, tuberous sclerosis and cerebral cortical calcification associated with vascular malformations (Sturge-Weber syndrome).

Recently we have encountered 2 cases of subtentorial intracranial calcification which had many features in common and offered some difficulty in analysis. In one case the findings on postmortem examination are presented. It was concluded that both cases represented calcification in the dentate nucleus and surrounding white matter of the cerebellum. While the clinical significance of this condition is not entirely clear, it is believed that the calcifications have no direct bearing on the patient's symptoms or physical findings.

In 1896 Mallory[3] reported finding calcified nodules in the dentate nucleus of the cerebellum during an autopsy of a case of chronic nephritis. He concluded that the precursor of this calcification was the accumulation of colloid material in the media of the larger arterioles and the infiltration of colloid in the capillary network, The end stage was atrophy of the nervous tissue in the area supplied by the affected vessels and formation of "sand-like deposits and stone-like concretions."

It is the general experience of pathologists, when sectioning brains routinely, that gritty deposits and concretions are commonly found, particularly in the older age groups. Despite its frequency on postmortem examination, roentgenologically symmetrical calcification of the basal ganglia in vivo was first described by Fritzsche[2] in 1935. Mention is made in this article of subtentorial calcification or calcification in the region of the dentate nucleus in 1 of 3 cases. In the 12 cases of symmetrical calcification of the cerebral basal ganglia reported by Camp,[1] 7 were associated with calcific deposits in the cerebellum, presumably in the dentate nucleus. The etiology of 11 of these cases was spontaneous parathyroid insufficiency. The remaining case had undergone a thyroidectomy. No case was reported with calcification only in the dentate nucleus. Rand, Olsen and Courville[4] also reported 2 cases of calcification of the dentate nucleus and basal ganglia. The majority of cases reported by Camp and by Rand had metabolic dysfunction or degenerative changes in the central nervous system.

The following 2 cases are of interest since the symmetrical calcification of the dentate nucleus was not associated with calcification demonstrable by roentgen

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examination of the basal ganglia or cerebrum. No definite etiology could be attributed to metabolic dysfunction or neurologic disease.

## REPORT OF CASES

Case 1 (No. 203813). J.R., white male, aged sixty-four. This patient was first seen in June, 1940, when he entered the Out-Patient Clinic of The Johns Hopkins Hospital with the complaint of sudden blindness. The family history was negative. The patient's past history disclosed that he had had the usual childhood diseases and "flu" in 1918. The present illness began abruptly on May 11, 1940. The patient said he suddenly went blind for a short period of time. Later, he complained of weakness of the legs, unsteadiness and difficulty of speech. He remained drowsy and uninterested in his surroundings.

Physical examination disclosed an undernourished white male of sixty-four years of age. His conversation was disconnected and he had marked difficulty in pronouncing words. Neurologic examination showed that tendon reflexes were absent and that the Romberg sign was positive. Routine laboratory studies revealed a positive serologic test for syphilis.

The patient was referred to the Syphilis Clinic where these additional findings were noted: The pupils were fixed; there was marked slurring of speech and evidence of mental deterioration. He was having active hallucinations. A slight tremor of the tongue and hands was noted. Both the knee and ankle reflexes were absent. Pressure sensibility was absent at the ankles. The ophthalmologist found no abnormalities in the fundi. A diagnosis of taboparesis was made.

Later, the patient entered the Baltimore City Hospital for fever therapy. A course of malaria treatment was given. The patient had ten chills after which his neurologic status was unchanged. Tryparsamide therapy was started but after five injections was discontinued because of reactions. Subsequently the patient became disoriented, had "fits" and, because of these, was committed to a mental hospital where he was again treated with malaria.

In February, 1942, he was seen again. The spinal fluid Wassermann reaction was still positive. Tryparsamide was once more tried, but was soon changed to bismuth in oil. He was next seen on October 21, 1947, following an automobile accident. Fractures of the skull, left ulna, the right ilium, the right tibia and fibula were found. The calcification in the posterior cerebral fossa was noted for the first time. The fractures were reduced and the patient admitted to the hospital. While on the ward, he was disoriented and required an indwelling catheter. After three weeks in the hospital, the fractures appeared to be healing and the patient was discharged to convalesce at home.

The final admission was on January 21, 1948, because the fractures failed to heal properly. Neurologic examination showed no essential change since 1942. Both the blood and the spinal fluid serologic tests for syphilis were still positive.

The patient's general physical condition was poor. At times he was disoriented and on one occasion had a mild cerebrovascular accident with sudden aphasia and weakness of the right arm. This condition cleared in forty-eight hours.

On February 18, 1948, pneumoencephalography was done. This examination showed considerable cortical atrophy and the calcification was demonstrated to be outside the ventricular system. The patient's course steadily deteriorated and death occurred on March 12, 1948.

No detailed neurologic examination was carried out during the patient's last admission to the hospital because of extensive casts and his poor mental state. As well as could be determined, however, no essential changes had occurred since 1942.

*Stereoscopic Films of the Skull.* The various projections (Fig. 1 and 2) revealed symmetrical dense serrated nodules of subtentorial calcification in the area occupied by the dentate nuclei. The calcification on the right measured 15 by 4 mm. and on the left 3 by 7 mm. There was a suggestion of very fine homogeneous calcification surrounding the discrete nodules. The bones of the sella, base and calvarium were within normal limits.

*Encephalogram.* Moderate cortical atrophy was noted in the left frontoparietal region. The ventricular system was well outlined and showed slight dilatation. Stereoscopic views showed no evidence of calcification in the fourth ventricle. The calcified masses appeared to be within the cerebellar substance.

*Impression.* Calcified deposits in the dentate nuclei.

Fig. 1. Case 1. Lateral roentgenogram of skull, retouched. Dense nodule of subtentorial calcification in the dentate nucleus situated at a point approximately equidistant from the internal occipital protuberance, the apex of the antral triangle and the posterior tip of the foramen magnum.

Fig. 2. Case 1. Occipital view of skull, retouched. Note symmetrical serrated calcification at a level midway between the foramen magnum and the external occipital protuberance.

*Postmortem Findings.* Gross: (Autopsy No. 21111, abstracted from Dr. Walker's report on the brain.) The convolutions were rounded and in the frontal regions were somewhat atrophied, more so on the left. The arachnoid was thickened and milky. Examination of serial coronal sections confirmed the cortical atrophy and revealed a marked dilatation of the ventricular system. There was no evidence of calcification in the choroid plexus or basal ganglia.

There was some resistance to the knife in making coronal sections through the cerebellum and, on palpation of the dentate nucleus, definite roughness was encountered. The white matter about the dentate nucleus was brownish in color and there was a mild injection of the vessels. In the white matter of the cerebellum on both sides posterior to the dentate nucleus there was an area which felt gritty and had a brownish color. This area measured 25 mm. in length and 6 mm. in width. It lay in the center portion of the cerebellum and did not extend to the peripheral folia. The choroid plexus appeared grossly normal (Fig. 3).

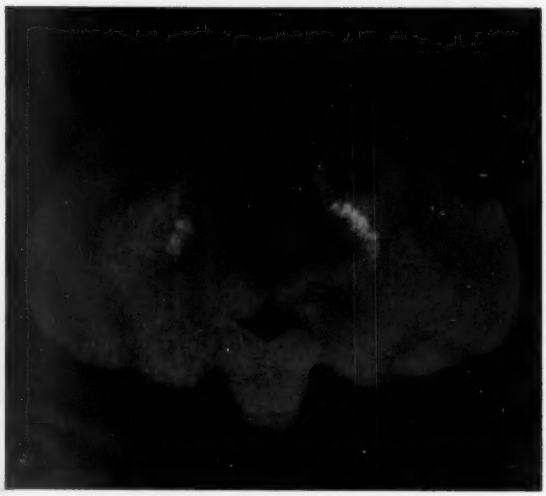

Fig. 3. Case 1. Roentgenogram of a coronal segment of brain through the cerebellum. The serrated, broad, white lines represent calcium deposits outlining the dentate nucleus.

*Microscopic Study.* Representative sections of frontal poles, rolandic fissure, calcarine fissure, striate region including head of caudate nucleus, thalamus, hippocampus, uncus, temporal lobes, midbrain, pons, medulla, cord and cerebellum

Fig. 4. Case 1. Cerebellum, low power magnification, ×14, hematoxylin and eosin stain. Note the dark masses of calcification surrounding especially the vascular structures.

were made. The leptomeninges were not remarkable. Occasional arteries showed intimal thickening by fibrous tissue.

Throughout the brain there was evidence of diffuse vascular disease, ranging from mild thickening of the walls of small arteries to various sorts of calcific deposits in the vessel walls. A moderate number of small arteries throughout the brain showed calcification of the medial layer of their walls.

In the cerebellum and to a much less extent in other regions of the brain, there were collections of round, calcified bodies ranging in size from less than 1 micron to 8 or 10 micra (Fig. 4 and 5). These deposits, which not infrequently coalesced, were in the walls and perivascular adventitial spaces of the blood vessels, as shown by reticulum stains (Fig. 6). This peculiar calcification was most conspicuous in the blood vessels of the granular layer and dentate nucleus of the cerebellum. In parts of these regions, it was extremely dense and almost every vessel appeared to be affected. The calcific bodies gave a positive reaction for both calcium and iron. So many of the vessels were involved in the region of the dentate nucleus that in stained sections the nucleus was easily visible to the naked eye and confirmed the roentgen appearance.

Other pathologic lesions in the brain were attributable to arteriosclerosis. There were patches of subpial and subependymal gliosis with numerous corpora amylacea. Surrounding some blood vessels in the cerebrum there was evidence of old destruction of the parenchyma.

It is remarkable that there was so little damage to the cellular elements of the cerebellum, despite the heavy deposits of calcium in the walls of numerous blood vessels. There was patchy gliosis in the granular layer but the vessels in this area were frequently not involved by the calcified deposits. The small vessels were rarely occluded by the calcified deposits, while the larger arteries often had narrowed lumens as a result of hyalinization of their walls together with the medial calcification.

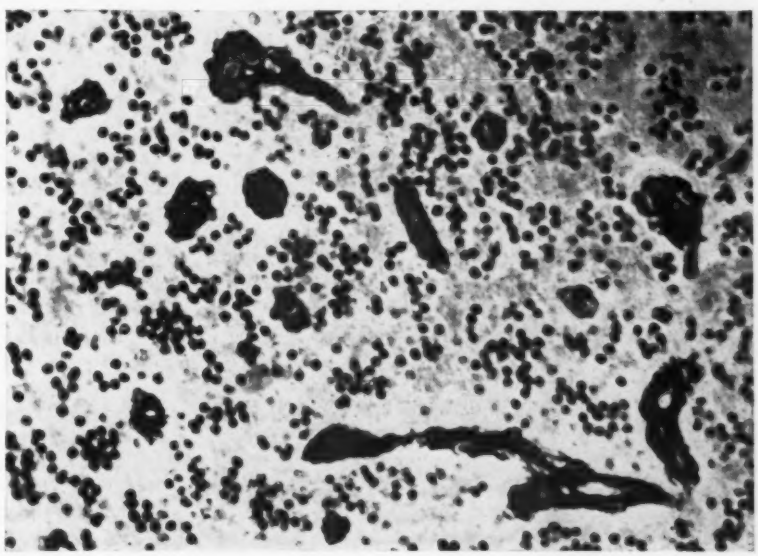

Fig. 5. Case 1. Cerebellum, high power magnification, ×580, hematoxylin and eosin stain. Note the dark masses of calcification surrounding the vascular structures.

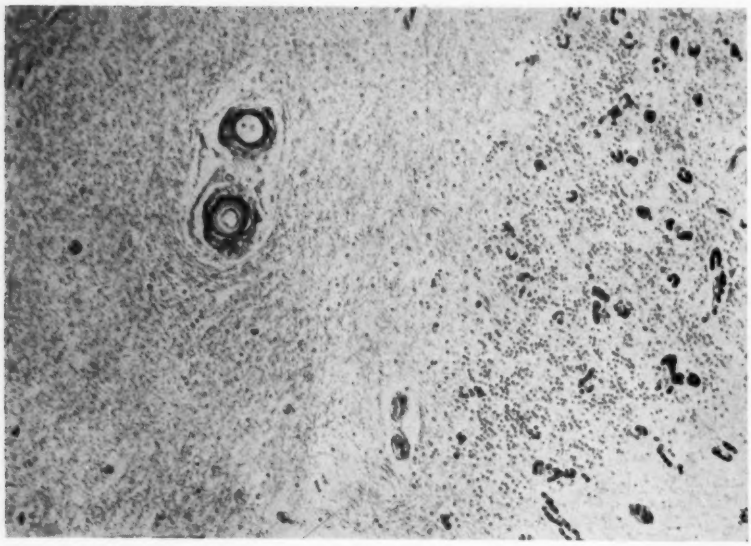

Fig. 6. Case 1. Cerebellum, low power magnification, ×175, hematoxylin and eosin stain. Note the calcification in the large vessels.

The Purkinje cells were not damaged except in the foci of gliosis that involved the folia. The dentate nucleus was well preserved. Calcified deposits were not seen in any other places except in close relation to the blood vessels.

Case II (No. 134220). A. P., white female, aged fifty-two. The patient was first seen in the Diagnostic Clinic of The Johns Hopkins Hospital in March, 1935. The family history revealed that two siblings had died about the age of forty of pulmonary tuberculosis. The patient had a past history of measles, mumps and chickenpox as a child. The patient had pneumonia three times within the last twenty years. She was said to have had St. Vitus' dance between the ages of one and three years. Thirty years ago the patient was said to have tuberculosis, but she had remained well without treatment.

The chief complaint was continual bilateral headaches in the occipital region extending into the neck for the past three years. Physical examination was essentially negative. The patient was studied intensively. Roentgenograms of the skull and long bones showed early Paget's disease. The neurologic examination was negative. At this time no mention was made of the calcification in the cerebellum.

The patient returned in February, 1939, because of frequent headaches. She was mentally upset and depressed. Again nothing definite was found.

When next seen on February 6, 1946, the patient had been admitted to the hospital with the complaint of dizzy spells of ten years' duration. Every one to three months she had had attacks of rotary vertigo with nausea and vomiting. These episodes lasted one to twelve hours. For the past three months, attacks had become more frequent, coming on almost daily. She had experienced tinnitis, described as as a "terrific buzzing" in the left ear three years previously when she had pneumonia. There was also a loss of hearing in that ear for the same length of time.

Physical examination showed a marked bowing of the right tibia. Neurologic examination showed a 30 per cent loss of hearing in the left ear. Bone conduction was absent on the left. A diagnosis of Ménière's disease was made.

Laboratory examination showed a negative serologic test for syphilis; calcium 11 mg., phosphorus 4.5 mg., non-protein nitrogen 36 mg., and a total protein of 7.15 gm. per 100 cc.

Roentgenograms of the skull now showed great density of the bones of the base compatible with Paget's disease. Bilateral symmetrical calcification was present in the cerebellum. On February 7, 1946, Dr. Dandy did a partial section of the left eighth nerve. The operative note remarks that the occipital bone was thick but very soft. The postoperative course was uneventful. The hearing remained unchanged. The tinnitis disappeared completely. Upon discharge, the patient still complained of dizziness, unsteadiness in walking and difficulty in fixing the field of vision.

The patient was seen again in September, 1947, at which time she still complained of unsteadiness. She said that she could not walk alone unsupported. The attacks of vertigo had ceased completely. If she turned quickly she would fall, unless she guarded herself. Neurologic examination showed only loss of equilibrium. She was unsteady with her eyes

open, and her unsteadiness was worse when they were closed. There was no ataxia or nystagmus. Roentgenograms of the skull showed no further changes. It was felt that the patient exaggerated her symptoms.

*Roentgenologic Examination.* Stereoscopic films of the skull showed dense calcification in the region of the pineal which appeared to be in the midline. There was thickening of the bones of the base of the skull as well as the calvarium and considerable osteoporosis of the occipital bone inferior to the nuchal line. In the posterior fossa, apparently in the substance of the cerebellum, in the region of the dentate nuclei, were two symmetrical coarsely linear calcific deposits with ill defined borders. The calcific deposits measured approximately 32 by 10 mm. bilaterally (Fig. 7 and 8).

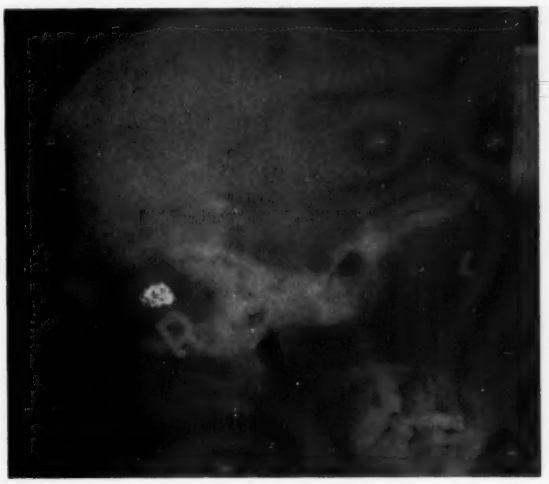

Fig. 7. Case II. Lateral roentgenogram of skull, retouched. Shows conglomerate, subtentorial calcification. There is also Paget's disease of the skull.

*Impression.* Paget's disease of the skull with osteoporosis circumscripta and calcification in the dentate nuclei.

## DISCUSSION

We have described 2 cases in which routine roentgenographic studies of the skull revealed calcification in the region of the dentate nuclei of the cerebellum. In Case I, postmortem roentgen examination of the cerebellum revealed dense serrated calcific deposits outlining perfectly the dentate nucleus. There was also fine

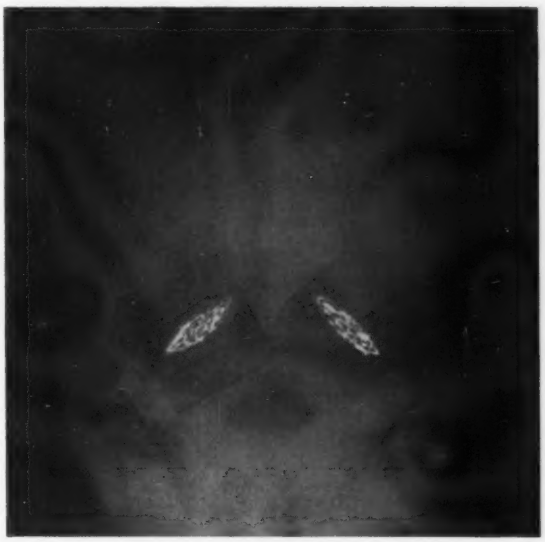

Fig. 8. Case II. Skull, occipital view, retouched. Note the coarse symmetrical masses of calcification in the posterior fossa.

linear calcification in the surrounding white matter.

Case I had central nervous system syphilis (taboparesis) which was treated by malaria. While Volland[5] and Weimann[6] discuss the possible relationship of calcification in the basal ganglia to syphilis and malaria, among other etiologic entities, they draw no definite conclusions.

Roentgenographically the possibility of calcification of the choroid plexus in the lateral recesses of the fourth ventricle may arise. The lateral recesses are small structures more medially placed than the dentate nuclei. Pneumoencephalography can definitely exclude this possibility, although no reference to it can be found in the literature nor have we encountered it in our experience.

Case II revealed more extensive calcification in the area occupied by the dentate nuclei. This patient had Paget's disease and Ménière's disease. Although the etiology of Paget's disease is unknown, we might postulate some derangement of calcium metabolism which produces the widespread bone changes and the frequent increase in alkaline phosphatase. Neither the numerous cases of Paget's disease

studied here roentgenographically nor the rather voluminous literature associate calcification of the dentate nucleus with this disease. Ménière's disease is also believed to be unrelated.

In both cases no symptoms or clinical findings could be ascribed to degeneration of the dentate nucleus. There are no clues in the patients' histories or physical examinations to indicate the etiology of the abnormal calcification.

In all of Camp's 12 cases which had parathyroid insufficiency, the most prominent feature was calcification in the cerebral basal ganglia. Two cases were associated with calcification in the dentate nucleus but none is cited with calcification in the dentate nucleus alone. Clinically, our 2 cases did not have hypoparathyroidism.

SUMMARY

Two cases are presented with calcification in the dentate nucleus and neighboring white matter of the cerebellum. These cases were not associated with calcification in the cerebral basal ganglia. We do not know the etiology and clinical significance of this type of calcification.

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REFERENCES

1. Camp, J. D. Symmetrical calcification of cerebral basal ganglia. *Radiology*, 1947, 49, 568–577.
2. Fritzsche, R. Eine familiär auftretende Form von Oligophrenie mit röntgenologisch nachweisbaren symmetrischen Kalkablagerungen in Gehirn, besonders in den Stammganglien. *Schweiz. Arch. f. Neurol. u. Psychiat.*, 1935., *35*, 1–29.
3. Mallory, F. B. Contribution to study of calcareous concretions in brain. *J. Path. & Bact.*, 1896, *3*, 110–117.
4. Rand, C. W., Olsen, C. W., and Courville, C. B. Gross calcareous deposits in corpora striata and dentate nuclei. *Bull. Los Angeles Neurol. Soc.*, 1943, *8*, 118–128.
5. Volland, W. Über Intracerebrale Gefässerkalkungen. *Arch. f. Psych. & Neurolkrank.*, 1940, *3*, 5–47.
6. Weimann, W. Über einen eigenartigen Verkalkungsprozess des Gehirns. *Monatschr. f. Psychiat. & Neurol.*, 1921, *1*, 202–234.

Vol. 67, No. 4

# DILATATION OF THE AZYGOS VEIN

## A ROENTGEN SIGN OF VENOUS ENGORGEMENT

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DILATATION of the neck veins is an easily discernible clinical sign of impaired backflow to the heart in instances of congestive failure, tricuspid insufficiency and pericarditis, both constrictive and with exudate. On the chest roentgenogram this venous engorgement is sometimes demonstrated by dilatation of the upper mediastinal shadow to the right, the structure of the superior vena cava itself being not distinctly discernible. Moreover, it is a fairly general experience that even this dilatation of the mediastinal shadow is not prominent in many instances. Several observations of marked dilatation of the azygos vein in instances of venous engorgement have led us to a more systematic study of this problem.

The normal azygos vein is roentgenologically often seen in children and with considerable frequency also in adults. The trunk of the azygos vein, formed by the junction of its lower stem and upper branch to the right of the esophagus, takes a horizintal course anteriorly above the right main bronchus and the other structures of the right hilum. The vein is usually closely attached to the trachea in the right tracheobronchial angle. The mediastinal pleura covering the trachea on the right deviates slightly to envelop the vein. The vein enters the superior vena cava at its posterior aspect, usually just before its entrance into the pericardial sac (Fig. 1).

The partially straight posteroanterior course of the azygos vein makes possible its axial projection on the routine chest film, where it stands out as a spindle-shaped shadow adjacent to the right tracheobronchial angle. The lower pole of this shadow is often rather plump; therefore the shadow is sometimes described as "pumpkin-seed" or "almond" shaped. Ottonello was the first to identify this shadow as azygos vein in 1932 (Fig. 2, Ottonello's original drawing).

In a review of 2,000 photofluorographic chest films of a survey, the azygos vein was found to be visible in more than two-thirds of all films. This figure refers to routine posteroanterior chest films. The right tracheobronchial angle lies sufficiently to the right to project often beyond the other mediastinal structures (Fig. 3). In many instances the azygos vein can be visualized

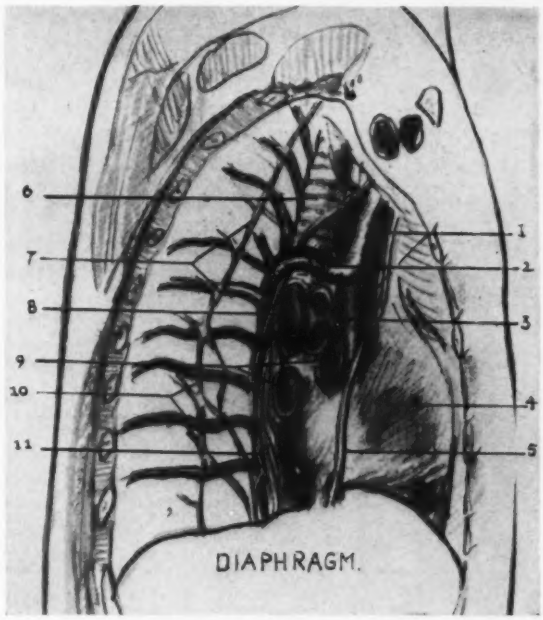


FIG. 1. Right lateral view of the mediastinum to demonstrate the topography of the azygos vein. *1*, superior vena cava; *2*, azygos vein; *3*, right pulmonary artery; *4*, heart covered by the pericardium; *5*, right phrenic nerve; *6*, trachea; *7*, sympathetic side chain and ganglia; *8*, right main bronchus; *9*, right superior and inferior pulmonary veins; *10*, intercostal veins; *11*, esophagus.

* From the Department of Radiology, Beth Israel Hospital and Harvard Medical School, Boston, Massachusetts. Presented before the Massachusetts Heart Association, March 6, 1950.

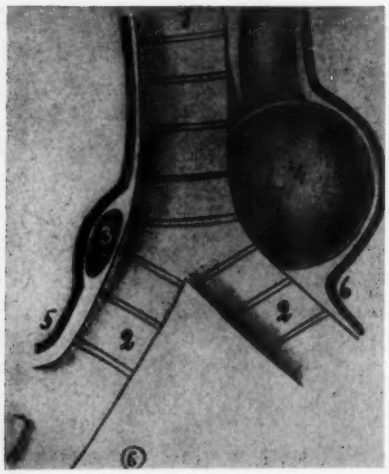

Fig. 2. Drawing from Ottonello illustrating the topography of the azygos vein in the posteroanterior view. *1*, trachea; *2*, main bronchi; *3*, azygos vein; *4*, aortic arch: *5* and *6*, mediastinal pleura.

on films taken with more penetration or with slight rotation toward the left oblique position. A narrow or wider spindle-shaped shadow in the right tracheobronchial angle is distinctly discernible. In other instances the azygos vein is clearly outlined in the right oblique position (Fig. 4). There are instances of clear exposure of the right tracheobronchial angle without any widening of the shadow band forming the tracheobronchial wall. The absence of the normal azygos shadow is fully explained in instances of an atypical lateral course of the vein with formation of an azygos lobe. In other instances it is not apparent whether there exists another anatomical abnormality such as described in anatomical texts or whether the azygos vein may collapse on deep inspiration to invisibility. Among anatomical variations, opening of the azygos vein into the right innominate (brachiocephalic) and into the right subclavian vein has been known. In rarer in-

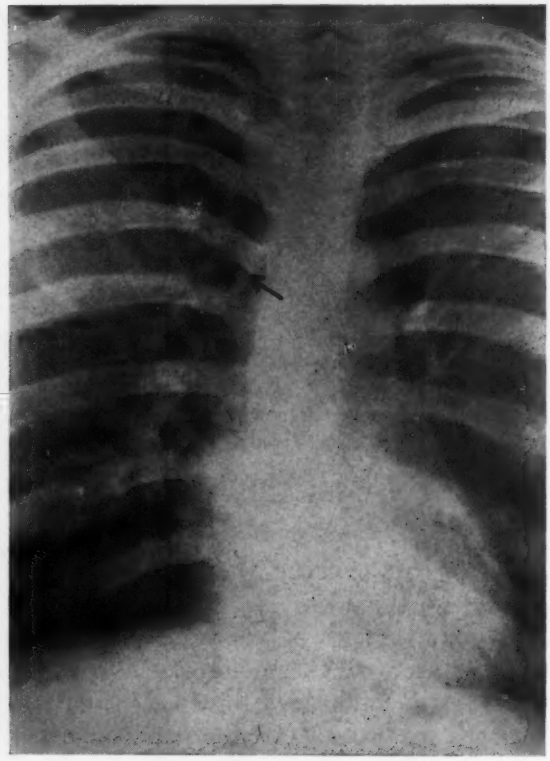

Fig. 3. Posteroanterior view of the chest of a healthy young woman. The shadow of the azygos vein in the right tracheobronchial angle is marked by an arrow.

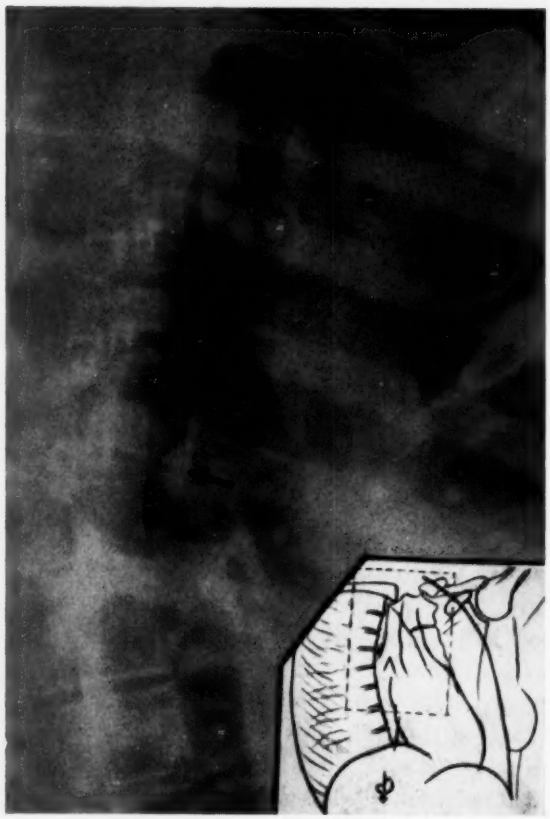

Fig. 4. Right oblique view in a healthy young woman. The shadow of the azygos vein in the right tracheobronchial angle is marked by an arrow.

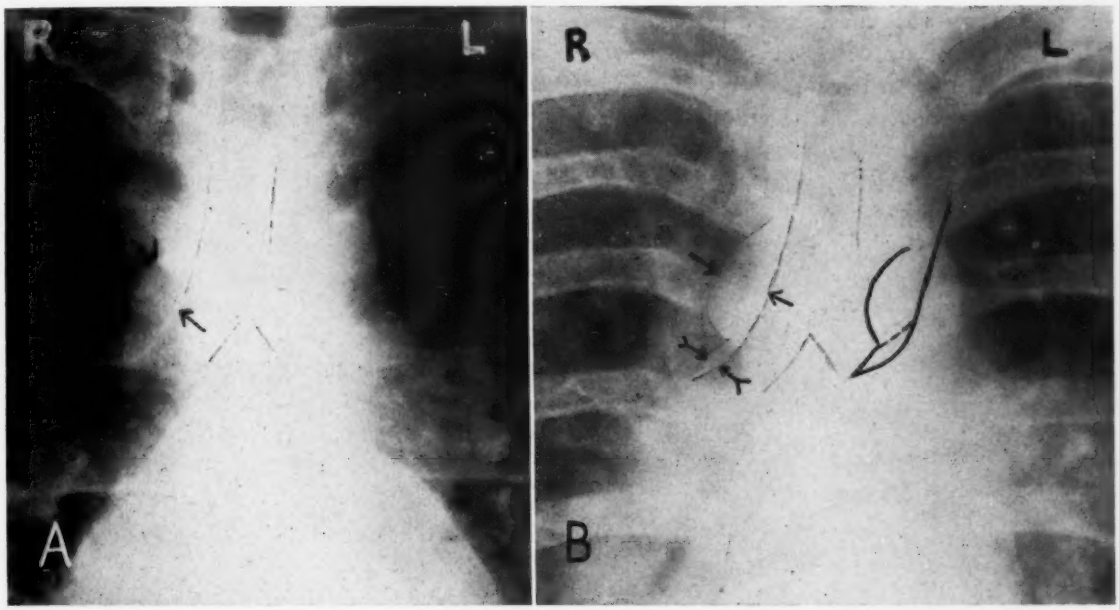


Fig. 5. (*A*) From a patient with constrictive pericarditis. The arrows point to the shadow of the widened azygos vein. Its lateral contour coincides with the contour of the dilated superior vena cava.

(*B*) From a patient with erythema nodosum and hilar and mediastinal lymphadenopathy. The upper plump shadow represents a lymph node, between simple arrows. The lower tail-like projection, between barbed arrows, is the azygos vein. An explanatory tracing of these structures has been placed to the left of the trachea. (Retouched)

stances the azygos vein may enter the pericardium and join the intrapericardial portion of the superior vena cava or the right auricle. In recumbent position there is often an increase in width of the venous shadow.

In subjects without cardiovascular disease we found this azygos shadow to have a width of up to 5 mm.; in rare instances 6 mm. The absolute width and changes of width of the azygos vein are not solely dependent on the intravenous pressure. The azygos vein, as an intrathoracic structure, is subject to the intrathoracic pressure. Since the effective intravenous pressure is the algebraic difference of the absolute venous pressure and the negative intrathoracic pressure, changes in the resilience of the lung, such as those occurring in pneumonia, fibrosis, the rigid lung in congestion (Lungenstarre) or extensive atelectasis, may influence the width of the azygos vein. Thus, if the pressure in the vena cava is measured +15 mm. $H_2O$, the intrathoracic pressure −60 mm. $H_2O$, the effective venous pressure is +75 mm. $H_2O$ (Wiggers). This relation is clearly brought out by the Valsalva experiment. In subjects with the azygos vein visible on roentgenoscopy, a decrease in width of the vein has been observed on forced expiration with the glottis closed.

Little attention has been given to the roentgen visibility of the azygos vein. Among the leading textbooks it is mentioned by Assman, Roesler and Zdansky. Durieu and Lequime observed changes of the width of the azygos shadow in instances of peripheral venous stasis. Our observations of venous congestion comprise instances of congestive heart failure, right ventricular strain, organic and functional tricuspid insufficiency, pericarditis, both constrictive and with effusion, and an instance of superior cava obstruction (above the junction of the azygos vein).

There are instances where it is difficult to distinguish the widened azygos vein from enlarged lymph nodes in the right tracheobronchial angle. Figure 5, *A* and *B*,

may illustrate this fact. The dilated azygos vein is spindle or diamond shaped, while an enlarged lymph node projects more in a semicircular fashion. The lateral contour of the azygos shadow coincides with the straight contour of the superior vena cava; moreover it makes the vena cava shadow recognizable as such by its presence. On the other hand, the vena cava shadow helps to identify the azygos shadow. No such relationship exists with an enlarged lymph node. The lymph nodes are often slightly higher in position while the azygos shadow fits snugly into the tracheobronchial angle (Fig. 5*B*). Decrease in width of the azygos shadow occurring during Valsalva's experiment, as well as increase during Müller's experiment or with change to the recumbent position, as mentioned above, may facilitate the distinction.

Furthermore, it is not intended to base far reaching clinical diagnoses and decisions on this limited observation. The widened azygos shadow on a routine chest roentgenogram goes parallel with and is documentary illustration of venous engorgement easily accessible to inspection of the neck veins; moreover, changes in width accompanying changes of venous pressure can be easily recorded. On the contrary, with isolated swelling of the right tracheobronchial node, in addition to the distinguishing features mentioned above, there will be absence of cardiovascular disease but possibly presence or suggestion of some kind of lymphadenopathy. Generally, this finding must be integrated in the clinical situation as a whole.

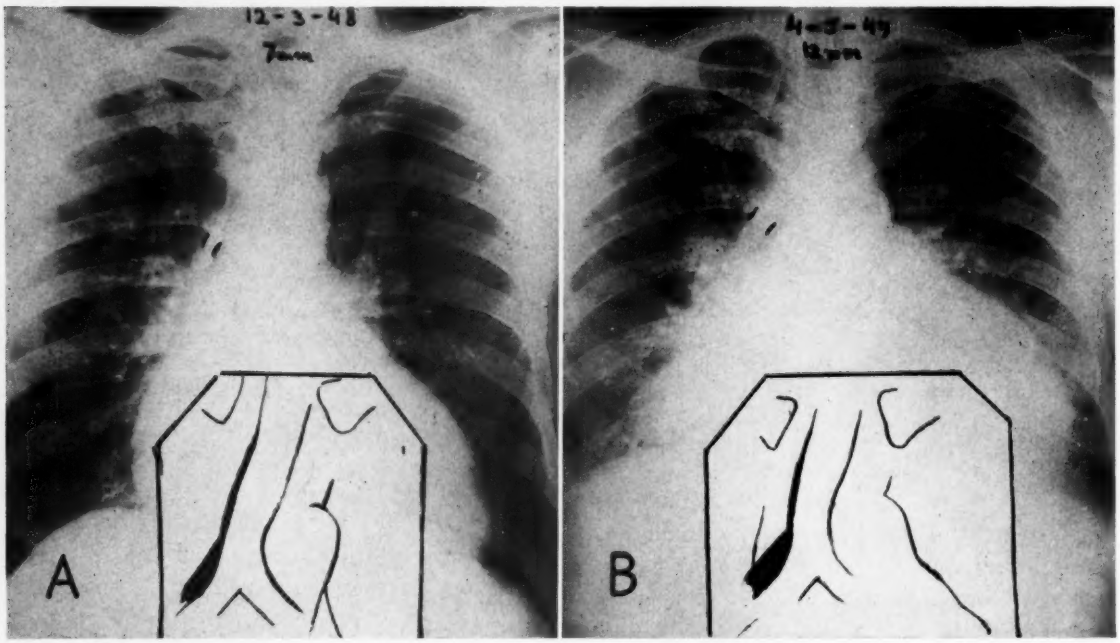


Fig. 6. Case 1. Rheumatic aortic and mitral disease. (*A*) Compensated: the azygos vein measured 7 mm. in width. (*B*) Four months later in congestive heart failure; the azygos vein measured 12 mm. (Retouched)

## Case Reports

Case 1. H.S., male, aged sixty-one, with a long history of rheumatic aortic and mitral valvular disease, was compensated when seen in December, 1948. The azygos vein measured 7 mm. in width (Fig. 6*A*). Four months later he had congestive heart failure with an enlarged, tender liver and engorged neck veins. At this time the azygos vein measured 12 mm. (Fig. 6*B*).

Case 11. M.K., female, aged forty-seven, with hypertensive heart disease, developed congestive heart failure with generalized ana-

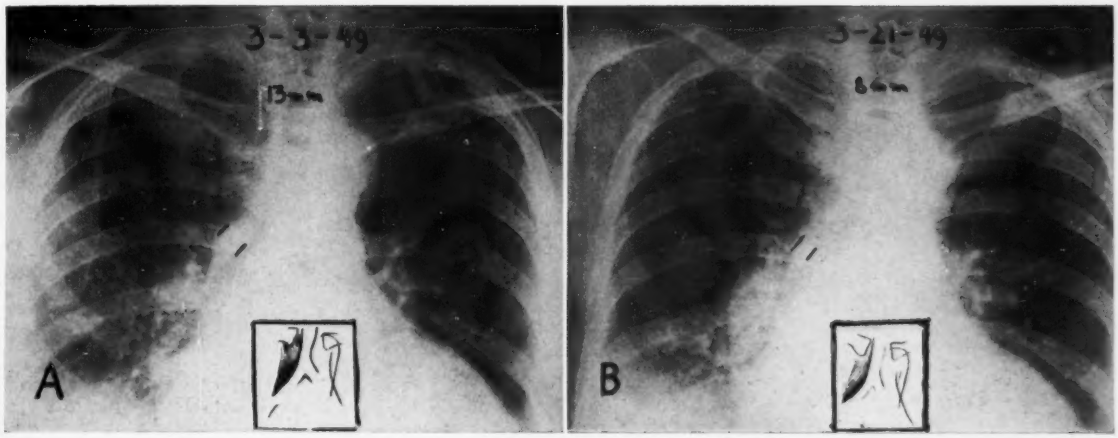


Fig. 7. Case II. (*A*) Hypertensive heart disease in congestive failure. Venous pressure 390 mm. water; azygos vein 13 mm. (*B*) Eighteen days later, marked clinical improvement; the venous pressure was 325 mm. water; the azygos vein measured 8 mm. (Retouched)

sarca after a hysterectomy. The width of the azygos vein was 13 mm. (Fig. 7*A*). Under diuretic treatment she improved with a concomitant weight loss of 51 lb. The width of the azygos vein decreased to 8 mm. during the first eighteen days of her observation (Fig. 7*B*).

Case III. R.F., female, aged fifty-five, had been treated by the Cardiac Clinic of the Beth Israel Hospital for hypertensive heart disease since 1943. In October, 1943, the azygos vein was 10 mm. in width (Fig. 8*A*). For several years her response to treatment was poor. In April, 1948, she received one dose of radioactive iodine, 25.5 mc. of $I^{131}$, with a striking therapeutic result. Eight months later, December, 1948, the azygos vein measured 4 mm. (Fig. 8*B*).

Case IV. H.T., male, aged twenty-three, had tuberculous polyserositis including pericarditis with effusion. Several paracenteses of the pleura and pericardium were performed. Because of signs of threatening cardiac tamponade, another pericardial paracentesis was performed on the eleventh hospital day with removal of 1,000 cc. of exudate and replacement with 200 cc. of air. Preceding this, the neck veins were markedly engorged, the venous pressure was 350 to 380 mm. citrate. Immediately after the paracentesis the patient felt greatly improved, the neck veins collapsed completely, the venous pressure fell to 170 mm. citrate. The azygos vein measured 8 mm. before (Fig. 9*A*) against 4 mm. immediately after the paracentesis (Fig. 9*B*). This case demonstrates, almost with the clarity of an experiment, the parallelism of clinical and roentgenologic observations.

Case V. P.M., male, aged sixteen, had polyserositis of unknown etiology for four years.

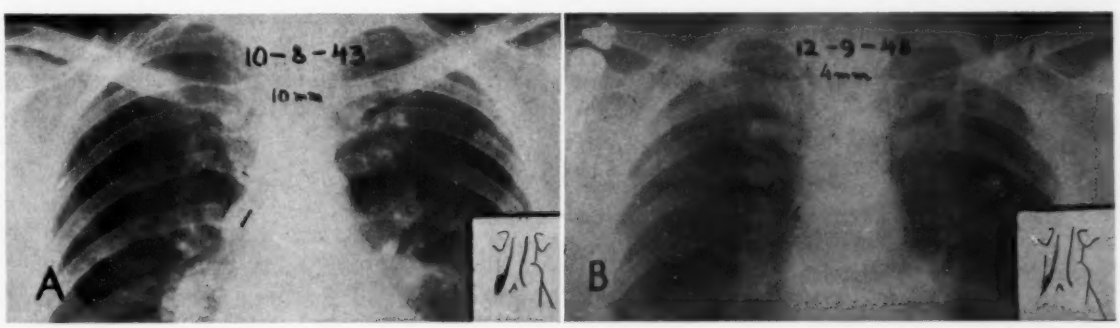


Fig. 8. Case III. (*A*) Hypertensive heart disease, in chronic congestive failure; azygos vein measured 10 mm. in 1943. (*B*) After treatment with radioactive iodine and general improvement, the azygos vein measured 4 mm. in 1948. (Retouched)

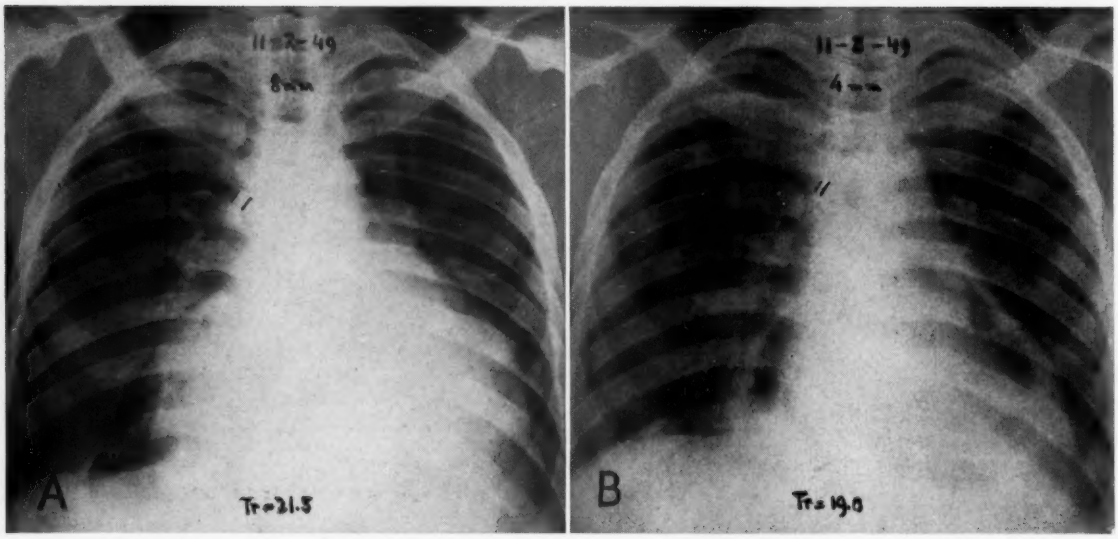


Fig. 9. Case IV. (*A*) Pericarditis with effusion; venous pressure 350 mm. citrate; azygos vein 8 mm (*B*) Immediately after pericardial paracentesis the venous pressure dropped to 170 mm. citrate; the width of the azygos vein to 4 mm. (Retouched)

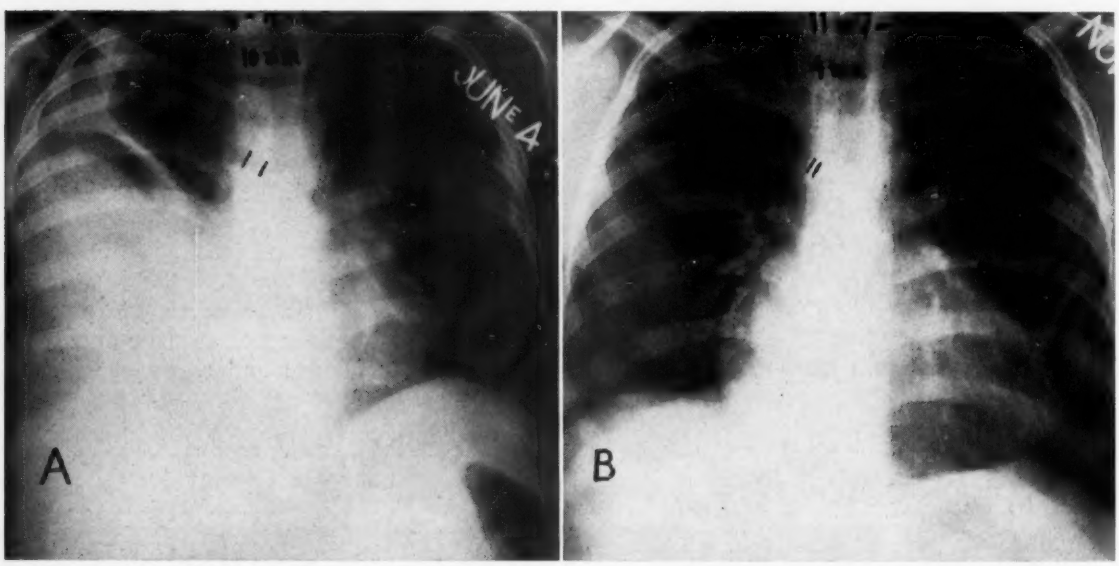


Fig. 10. Case V. Constrictive pericarditis with pleural and peritoneal effusion. (*A*) Before the pericardial decortication the azygos vein measured 10 mm. (*B*) After the operation 4 mm. (Retouched)

When readmitted to the hospital in June, 1946, he had evidence of calcific constrictive pericarditis. The azygos vein measured 10 mm. (Fig. 10*A*). He was successfully operated on by Dr. Richard Sweet on July 23, 1946. Four months later, when completely recovered, the azygos vein measured 4 mm. (Fig. 10*B*).

## SUMMARY AND CONCLUSIONS

The azygos vein is visible on about two-thirds of routine chest roentgenograms. It can be rendered visible in more instances by the use of increased penetration with or without the Potter-Bucky diaphragm, and

also by slight rotation toward the left or right oblique position.

The azygos vein appears as a spindle-shaped shadow in the right tracheobronchial angle. In subjects without cardiovascular disease the width of the azygos shadow (plus the wall of the trachea) is usually 5 mm. or less, in rare instances up to 6 mm. In instances of peripheral venous stasis the azygos shadow is usually wider. Improvement or deterioration of the peripheral venous circulation, as recognized by engorgement of the neck veins and venous pressure, are well reflected in changes of the width of the azygos vein shadow.

Observations of these changes, improvement and deterioration, in instances of congestive heart failure, pericarditis with effusion and constrictive pericarditis are presented. Dilatation of the azygos vein was also regularly found in tricuspid insufficiency and in one instance of obstruction of the superior vena cava above the junction of the azygos vein; it should be expected also in tricuspid stenosis.

The width of the azygos vein can be measured and recorded, and lends itself to objective comparison. It appears to be a useful indicator of the functional integrity or impaired performance of the right heart; in other rarer instances, the dilated azygos vein signalizes impaired inflow due to pericardial disease, or collateral circulation in obstruction of the vena cava.

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REFERENCES

1. Assman, H. Die klinische Röntgendiagnostik der inneren Erkrankungen. Fifth Edition. F. C. W. Vogel, Berlin, 1934.
2. Durieu, H., and Lequime, J. Aspects radiologiques de la veine azygos au cours de l'insuffisance cardiaque. *Arch. d. mal. du coeur*, 1938, *31*, 609–617.
3. Ottonello, P. Bemerkungen zur normalen Röntgenanatomie des Thorax. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1932, *45*, 677–687.
4. Roesler, H. Clinical Roentgenology of the Cardiovascular System. Second edition. Charles C Thomas, Publisher, Springfield, Illinois, 1943.
5. Wiggers, C. J. Physiology in Health and Disease. Lea & Febiger, Philadelphia, 1949.
6. Zdansky, E. Roentgendiagnostik des Herzens und der Gefaesse. Second edition. Julius Springer, Wien, 1949.

# ROENTGENOLOGIC FINDINGS ACCOMPANYING CARCINOMA OF THE PANCREAS*

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THE value of roentgenologic examination of the stomach and duodenum, if patients are suspected of having carcinoma of the pancreas, has been mentioned in numerous articles. The authors of some of these articles themselves seem slightly incredulous as to the percentage of positive findings.

It is well known that carcinoma of the pancreas frequently is not recognized until resection has become impossible. Early nodal metastasis, impingement on the greater blood vessels and perineural involvement are developments, the evidences of which all too frequently are seen at the time of surgical operation, and which contribute to the terrible mortality of this condition. Carcinoma in the region of the ampulla of Vater is recognized earlier than is carcinoma in the pancreas because, owing to its site, the former is more likely to obstruct the common bile duct and produce jaundice; furthermore, it is much more likely to be resectable because of its smaller size, later metastasis, and less frequent involvement of blood vessels.

As Miller and co-workers[15] have pointed out, investigations usually have been concerned mainly with necropsy material and the very important preicteric stage has not been emphasized. However, roentgenologic examination of the stomach and duodenum, made in the course of this phase, might establish a diagnosis and allow the surgeon to perform radical resection, thus offering the patient his *only* chance of survival. This is the stage when the patient notes loss of weight and progressive weakness, and it occurs about six months prior to the onset of jaundice. Most patients, moreover, complain of epigastric pain which extends to the back and is constantly present for at least two to three months before jaundice develops.

Because, under any circumstances, the pancreas cannot be visualized directly, it is necessary to obtain second hand information concerning any malignant growths within it and this is most easily done by roentgenologic examination of the stomach and duodenum after the taking of a barium meal. As early as 1923, Dickson described deformities of the stomach and duodenum which he thought might be attributable to carcinoma of the pancreas. Butler and Ritvo, in 1931, reported widening of the duodenal loop secondary to enlargement of the head of the pancreas, and Rigler two years later confirmed their work and also reported the deformity produced by carcinoma of the body and tail of the pancreas. Engel and Lysholm, in 1934, reported their method of studying the size of the pancreas by taking lateral films of the abdomen with the patient prone after employing effervescing powder to produce gas in the stomach. Enlargement of the pancreas could be determined by measuring the width of the shadow of soft tissue that lay just anterior to the upper lumbar portion of the spinal column, as this shadow contrasted with the translucent gas-filled stomach which lay still more anteriorly. In 1938 Frostberg described a "reverse three sign" which was a deformity seen in the second portion of the duodenum in the region of the ampulla.

* Presented at the Fifty-second Annual Meeting, American Roentgen Ray Society, Washington, D. C., Sept. 25–28, 1951.

This sign was characteristic not only of carcinoma of the head of the pancreas, but also of pancreatitis and simple edema. Many other individuals have published articles on the roentgenologic aspects of pancreatic carcinoma, particularly Case, whose article is a classic, and Poppel,[17] whose book covers very thoroughly all aspects of pancreatic disease.

In order to obtain the true numerical representation of the effectiveness of roentgenologic examination in this condition, it would be necessary to include not only cases in which the roentgenologic diagnosis had been proved at surgical operation and at necropsy, but also all cases in which roentgenologic findings had been positive but in which surgical operation or necropsy was not done. Obviously this last group cannot be adequately studied and investigators must be satisfied with study of roentgenologically positive cases in which surgical exploration or postmortem examination was performed. This is the type of study that has been done in the past, and Berk, in reporting his own series of cases and summarizing 10 previously reported series, found an over-all average of 37 per cent of cases in which results of roentgenologic examination were positive or suggestive in a total of 367 cases in which the diagnosis was proved. Ransom has reported the largest number of cases (93) in which the condition was proved to be present, in 25 per cent of which the roentgenologic findings were positive. MacKinnon had the highest percentage (71) of positive findings in 21 proved cases.

Our own investigation was prompted partly by the reports of the experience of others which has been cited in preceding paragraphs but primarily by the recent reports of surgeons. In 1935, Whipple and associates employed radical pancreatoduodenectomy for carcinoma of the ampulla of Vater, and several years later this same procedure was used by Brunschwig for carcinoma of the head of the pancreas. More recently, heartening reports have been made.[14,15] It is hoped that an increasing number of five year survivals will result from improved surgical skill and earlier preoperative diagnosis, especially diagnosis in the preicteric period.

With these rays of hope in a situation which otherwise carries a completely dismal prognosis, we reviewed Mayo Clinic records of cases in which the diagnosis of carcinoma of the pancreas was made at the time of operation during the four year period from 1944 through 1947. From this series we selected for study the 167 cases in which the upper part of the gastrointestinal tract had been examined roentgenologically. It is on this material that this article is founded. We excluded cases of carcinoma of the ampulla of Vater and of the second portion of the duodenum; they will be the subject of a later report.

## PATHOLOGY

Carcinoma of the pancreas makes up from 1 to 2 per cent of all carcinomas. The neoplasm is usually firm and of an infiltrative nature, and in about three-fourths of the cases in which biliary obstruction is present, there is associated chronic pancreatitis. The head of the pancreas is the most frequent site of carcinoma. Berk, in a collected series of 1,449 cases, found that the head was involved in 81 per cent; and the corresponding figure reported by Rives and collaborators, concerning their collected series of 415 cases, was 66 per cent. The sites of involvement in our series of cases are represented in Table 1.

Necropsy has disclosed that frequently the tumor is adherent to the duodenum and less often to the stomach. Grauer, Rives and associates and Kauer and Glenn all have demonstrated this. Malignant ulceration in the duodenum also has been found frequently at necropsy, although discusssion of it has been minimal in the roentgenologic literature. In a review of seventeen articles, Kauer and Glenn found that a tumor had been palpable in from 6 to 60 per cent of cases.

It is well known that the mass of pancreatic carcinoma is responsible for certain

Table I

SITE OF PANCREATIC CARCINOMA

| Portion of pancreas | Roentgenologically | | Total cases |
|---|---|---|---|
| | Positive, cases | Negative, cases | |
| Head | 50 | 58 | 108 |
| Body | 3 | 14 | 17 |
| Tail | 1 | 1 | 2 |
| Head and body | 4 | 0 | 4 |
| Body and tail | 2 | 6 | 8 |
| Diffuse | 10 | 13 | 23 |
| Total | 70 | 92* | 162* |

* In 5 cases data as to site were not available.

roentgenologic findings, but it is less widely known that actual invasion of the stomach or duodenum plays as important a part in production of positive roentgenologic findings. Miller, Baggenstoss and Comfort found that the mean diameter of 144 carcinomas of the head of the pancreas was 4.2 cm., while the mean diameter of 58 carcinomas situated in the body and tail was 5.6 cm. In Table II are recorded the various sizes of the lesions as determined from operation or from the surgical specimens that were examined in the course of our study. It is important to note that in many of the cases in which the roentgenologic findings were positive, the tumors were very small,

Table II

SIZE OF PANCREATIC CARCINOMA

| Diameter, cm. | Roentgenologically | | Total cases |
|---|---|---|---|
| | Positive, cases | Negative, cases | |
| 2 to <4 | 6 | 7 | 13 |
| 4 to <6 | 6 | 7 | 13 |
| 6 to <8 | 5 | 8 | 13 |
| 8 to <10 | 0 | 1 | 1 |
| 10 to <12 | 2 | 3 | 5 |
| 12 to 15 | 2 | 3 | 5 |
| Total | 21 | 29 | 50* |

* Unable to obtain data in the remaining cases.

57 per cent being less than 6 cm. in diameter. Frequently, therefore, it is a combination of the two factors, mass and invasion, which produces the alteration.

In reviewing the reports of operation or necropsy in the 70 cases in which roentgenologic examination gave a positive result, we found that in 49 cases carcinomatous tissue had been obtained. In 24 cases biopsy of the pancreas itself gave a positive result. In 14 cases biopsy was made of a metastatic nodule from the liver; positive lymph nodes were found in 5 cases; tissue from the omentum was found to be malignant in 3 cases, and tissue from the duodenum in 3. In all the remaining cases of the 70, at the time of surgical operation an enlarged, hard pancreas was observed and the surgeon established the diagnosis of carcinoma of the pancreas. In all of the cases in which tissue was available, the microscopic diagnosis was adenocarcinoma. According to the method of Broders, the malignancy in 5 cases was graded 1; in 21 cases, 2; in 13 cases, 3 and in 10 cases, 4.

## ROENTGENOLOGIC FINDINGS

In order to estimate the diagnostic accuracy of roentgenologic examination of the upper part of the gastrointestinal tract, we divided into two groups the 167 cases of carcinoma of the pancreas in which such examination had been made. The first group consisted of 70 cases in which the roentgenologic diagnosis indicated some abnormality in relation to the stomach or duodenum, and although the exact pathologic diagnosis was not made in many instances, the findings were considered to be satisfactory and of a positive nature. The second group was composed of 97 cases in which the result of roentgenologic examination was negative or in which the findings were not pertinent or suggestive of the underlying pancreatic lesion.

The technique used in roentgenologic examinations of the stomach and duodenum at the Mayo Clinic has been described previously.[23] Suffice it to say that roentgenoscopic examination is the primary proce-

dure and roentgenograms are a useful adjunct. We used no special methods or positions.

Of the 70 cases in the first group we found roentgenologic involvement of the stomach in 11 instances. The stomach and duodenum together were involved in 10 cases, while the duodenum alone showed roentgenologic changes in 49 instances (70 per cent). The first portion of the duodenum was the most frequent location to show these changes, the first and second portions together were the next most common site, and the second portion alone was the third most common spot. It is the duodenum, therefore, that particularly should be watched in any suspected case of pancreatic malignancy.

The roentgenologic criteria for the diagnosis of carcinoma of the pancreas have been discussed thoroughly,[7,9,11,16,17,20] and our findings are listed in Table III. On roentgenologic examination of the stomach and duodenum, carcinoma of the pancreas may make itself manifest in the following manner:

1. The carcinoma may be of sufficient size to be palpated in the course of roentgenoscopy, and because of its mass it may distort, obstruct, narrow, or produce a filling defect in any portion of the stomach or duodenum, depending on the site of origin of the carcinoma in the pancreas. Case clearly summarized these changes. Of our series, in 26 of the 70 cases in which roentgenologic examination gave a positive result, there was said to be a mass extrinsic to the stomach and duodenum, and in 9 of these 26 cases the mass was reported to be pancreatic in origin. In only 8 cases (16 per cent) was the "typical" widening of the duodenal loop seen, and we believe, as did Paul, that this is *not* a frequent finding in the condition.

2. The carcinoma may deform the stomach or duodenum. Such deformity, especially of the duodenum (Fig. 1 to 7 inclusive), was the most frequent finding in our cases.[14] The defect usually appeared on the concave aspect of the first or second parts of the duodenal loop and the irregularity usually was localized to a small segment. At surgical operation, this was found to be attributable, in the vast majority of instances, to actual invasion of the wall of the bowel, distortion owing to adhesions, or alteration of the normal anatomic structure by the mass of the tumor. Deformity was noted in 43 cases: in 3 it was of the pyloric end of the stomach; in 14, of the first portion of the duodenum; in 12, of the second portion; in 6, of both the first and second portions; in 5, at the junction of the first and second parts; in 1, of the third part; in 1, of the fourth part, and in 1, of the entire duodenum.

The tumor may produce obstruction either by exerting external pressure, and thus narrowing the lumen of the duodenum or pylorus, or by invading the submucosa or mucosa of the intestine. The nature of the underlying lesion is then difficult to de termine, depending, of course, on the degree of obstruction. The obstruction produces dilatation of the duodenum or stomach orad

Table III

ROENTGENOLOGIC MANIFESTATIONS IN 70 CASES OF CARCINOMA OF THE PANCREAS

| Roentgenologic feature | Incidence* |
|---|---|
| "Deformity" | |
| Pylorus | 3 |
| Duodenum | 40 |
| Filling defect | |
| Stomach | 7 |
| Duodenum | 11 |
| Obstruction | |
| Pylorus | 2 |
| Duodenum | 14 |
| Ulceration | |
| Pylorus | 1 |
| Duodenum | 13 |
| Narrowing | |
| Duodenum 1st part | 11 |
| Duodenum 2nd part | 2 |
| Dilatation | |
| Stomach | 6 |
| Duodenum | 7 |
| Wide loop | 8 |
| Fixation | 2 |

* More than one manifestation occurred in each of many cases.

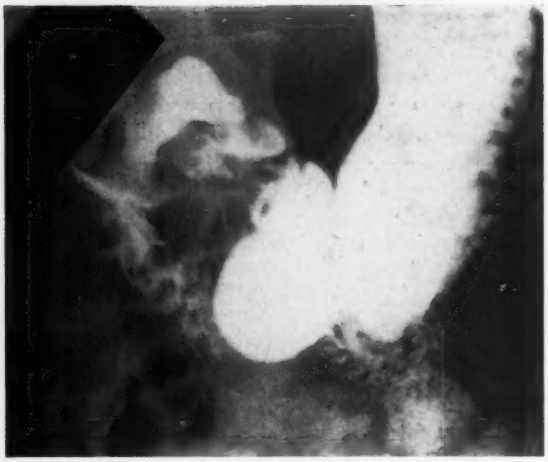

Fig. 1. Woman, aged forty-three. Adenocarcinoma Grade 4 arising from head of pancreas and infiltrating first and second portions of duodenum. Roentgenogram: ulceration and deformity of duodenum.

to the lesion, the degree depending on the severity of obstruction.

A filling defect is best seen in the presence of those lesions of the body and tail of the pancreas which, because of their mass, produce by pressure a smooth indentation of the lesser or greater curvature of the stomach. This is clearly evident when the patient is in position for the lateral projection. Diffuse involvement of the pancreas also will produce this manifestation. In 2 cases of carcinoma, in 1 of which the neoplasm was in the body, and in the other in the tail, of the pancreas, the defect was indicative of mucosal irregularity, with ulceration and narrowing of the lumen resulting from infiltration by malignant tissue. In both of these cases, the roentgenologic features resembled closely those of primary carcinoma of the fourth portion of the duodenum.

As has been pointed out,[23] the changes seen at the time of roentgenologic examination represent merely the gross morphologic features of the lesion. In our cases the deformity or filling defect usually involved a short segment of the bowel, was rather sharply demarcated, and frequently the mucosal pattern was altered or obliterated. Primary malignant growths of the ampulla of Vater and of the duodenum give this same roentgenologic appearance. Since lesions of the papilla of Vater, of the head of the pancreas, and of the duodenum near the biliary papilla all may arise within 0.5 cm. of each other, roentgenologic differential diagnosis frequently may be impossible. Benign ulcer of the first or second portion of the duodenum must also be considered in the differential diagnosis.

### Coexistence of Duodenal Ulcer and Carcinoma of the Pancreas

As Dashiell and Palmer have pointed out, the existence of pancreatic carcinoma may be unsuspected because of roentgenologic evidence of apparent duodenal ulcer and a clinical picture suggestive of peptic ulcer. Bockus expressed the belief that 12 per cent of patients with carcinoma of the pancreas will give a clinical picture of peptic ulcer. It is important, therefore, for the clinician to keep this in mind because reexamination of the stomach and duodenum

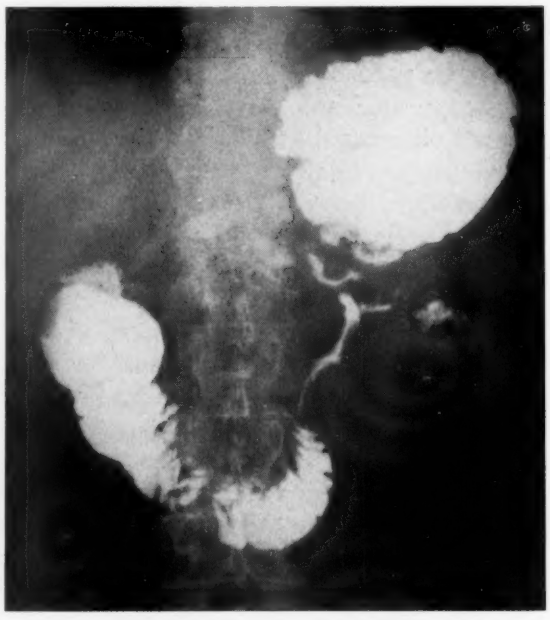

Fig. 2. Woman, aged seventy-four. Malignant involvement of tail of pancreas. Roentgenogram: constriction and obstruction of fourth portion of duodenum and ulceration of the mucosa; note resemblance to shadow seen in primary malignancy of duodenum.

four to eight weeks after the previous examination may disclose additional roentgenologic signs of pancreatic tumor. This was true in 4 cases in our series, and we feel that this is an especially important point in early diagnosis.

We found 23 cases supposedly of duodenal ulcer among the 167 cases under discussion, or an incidence of 13.8 per cent. On review of these 23 cases, however, we found 11 in which the duodenal deformity was interpreted as being caused by a duodenal ulcer and was reported as such, but findings at surgical operation or necropsy disclosed that the deformity resulted from the pancreatic lesion. Thus the incidence of duodenal ulcer among the 167 cases became 7.2 per cent and is not significant.

Fig. 3. Man, aged sixty-six. Adenocarcinoma Grade 3 of head of pancreas and metastasis to liver. Roentgenogram: narrowing and pressure deformity on inner aspect of second portion of duodenum.

### Correlation between size of tumor and positive roentgenologic findings

We recorded the diameter of the tumor as mentioned in the surgical report or as determined by examination of the gross specimen. In Table II is given the size of the carcinoma in cases in which we were able to measure the tumor. Although a tumor of the head measured only 2 to 3 cm. in diameter in some instances, there

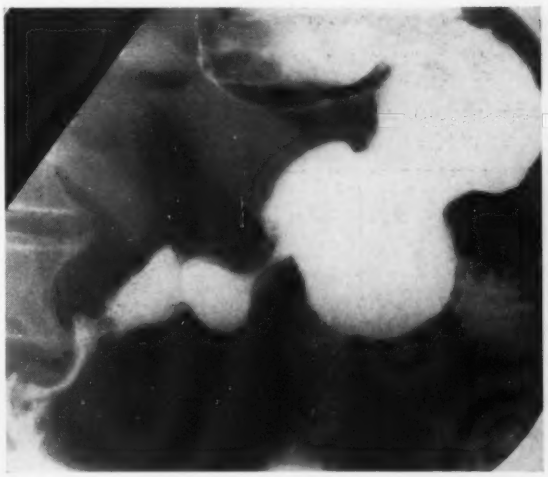

Fig. 4. First roentgenologic study (not represented here): suggestive of either primary duodenal malignancy or duodenal involvement secondary to carcinoma of pancreas. Second roentgenologic study, made on day after first (represented here): favorable to latter of the possibilities recognized on previous day. Constriction of first and second portions of duodenum, shown here, was secondary to a lesion, 5 cm. in diameter, in head of pancreas.

Fig. 5. Man, aged forty-one. Roentgenogram: filling defect in duodenum in region of ampulla of Vater; alteration of mucosal pattern and dilatation of duodenum above lesion. Surgical operation: radical pancreatoduodenectomy (Whipple) for adenocarcinoma Grade 3, 2.5 cm. in diameter, of head of pancreas, which had invaded the mucosa of the the second part of the duodenum and produced ulceration.

Fig. 6. Man, aged thirty-six. Adenocarcinoma Grade 4, 6 cm. in diameter, of head of pancreas. Roentgenogram: a rather long constricting lesion of second part of duodenum, with loss of normal mucosal pattern. Surgical operation: partial gastrectomy and duodenectomy.

were positive roentgenologic findings, while in some cases in which the carcinoma in the head was 12 to 15 cm. in diameter roentgenologic examination gave a negative result. When the head of the pancreas is the site of the tumor, the close proximity of the duodenum leads to invasion or pressure deformities much more readily than when the lesion is in the body or tail. Usually a tumor in either of these latter sites must be large if it is to make its presence evident in examination of the stomach.

It has been felt in the past that palpability of the tumor at the time of roentgenoscopy is a major factor in determination of the extrinsic nature of a lesion. As can be inferred from Table II, some of these tumors were so small that they could not be palpated and dependence had to be placed on the indirect signs already mentioned. It is in this group that we feel the roentgenologist may offer the greatest help. As Miller and others[15] have pointed out, the presence of a large, palpable pancreatic tumor and jaundice means that probably only a palliative surgical operation can be done, while the early, small carcinoma may be amenable to a radical surgical procedure and the patient may have a chance for prolongation of life or cure.

In our series were 9 cases in which the Whipple, or radical, pancreatoduodenectomy was performed. In 8 of these, roentgenologic findings were positive. In 1 case of the 8 the condition was interpreted as carcinoma of the pancreas or duodenum; in 1 case, "tumor of the pancreas"; in 2 cases, "carcinoma of the pancreas and/or duodenal ulcer"; in 2 cases an "obstructing lesion" was reported, and finally, in 2 cases deformity of the second portion of the duodenum was described but no suggestion was offered as to the cause.

Thus, among patients who were seen early enough to have the benefit of radical surgical operation, the roentgenologic findings relative to all but 1 were of great diagnostic aid, and although the tumors usually were small, a fairly accurate impression was obtained. The fact that a precise

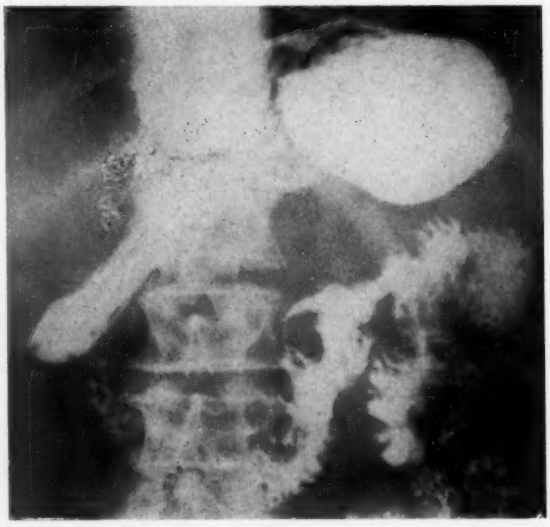

Fig. 7. Man, aged seventy-one. Adenocarcinoma Grade 3 of body of pancreas. Roentgenogram: deformity of fourth portion of duodenum and mucosal irregularity. Preoperative diagnosis: "probably carcinoma of the fourth portion of the duodenum."

pathologic diagnosis cannot be made in all cases should not discourage the use of roentgenologic examination, for the presence of a lesion can at least be recognized, its location can be noted and the clinician and surgeon thus can be given valuable aid in establishing a preoperative diagnosis.

## COMMENT AND SUMMARY

With the recent encouraging note in the results of radical pancreatoduodenectomy for carcinoma of the pancreas, the focus of attention is on the earliest possible preoperative diagnosis. Roentgenologic examination of the stomach and duodenum is one of the most useful adjuncts and in this series of 167 cases of carcinoma of the pancreas in which this examination was made, roentgenologic findings were positive in 70 cases (41.9 per cent).

A malignant growth in the head of the pancreas, invading the first portion of the duodenum, may give a roentgenologic picture which simulates that of duodenal ulcer and costly delay in making the correct diagnosis may result. Duodenal ulcer and carcinoma of the pancreas occurring in the same case were found in 7.2 per cent of our series and we believe this incidence of coexistence is not significant.

In cases of carcinoma of the head of the pancreas, the small operable lesions will give positive roentgenologic findings just as frequently as the large and frequently inoperable ones, the defect usually being attributable to invasion of the duodenum by the malignant process.

In 9 cases in this series radical pancreatoduodenectomy was performed. In 8 of these, roentgenologic examination of the duodenum gave a positive result. In the preicteric stage of the disease, the radiologist may greatly aid in early diagnosis, thus demonstrating the need of radical surgical operation, which is the patient's only hope for survival.

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## REFERENCES

1. BERK, J. E. Diagnosis of carcinoma of pancreas. *Arch. Int. Med.*, 1941, *68*, 525–559.
2. BOCKUS, H. L., and others. Gastro-Enterology. W. B. Saunders Company, Philadelphia, 1946, Vol. III.
3. BRUNSCHWIG, A. Resection of head of pancreas and duodenum for carcinoma-pancreatoduodenectomy. *Surg., Gynec. & Obst.*, 1937, *65*, 681–684.
4. BUTLER, P. F., and RITVO, M. Extra-bowel pathology. AM. J. ROENTGENOL. & RAD. THERAPY, 1931, *25*, 474–481.
5. CASE, J. T. Roentgenology of pancreatic disease. AM. J. ROENTGENOL. & RAD. THERAPY, 1940, *44*, 485–518.
6. DASHIELL, G. F., and PALMER, W. L. Co-existence of pancreatic carcinoma and duodenal ulcer. *Gastroenterology*, 1947, *9*, 773–777.
7. DICKSON, W. H. Diagnosis of obscure abdominal lesions by roentgen gastrointestinal examination. AM. J. ROENTGENOL. & RAD. THERAPY, 1923, *10*, 540–546.
8. ENGEL, A., and LYSHOLM, E. New roentgenological method of pancreas examination and its practical results. *Acta radiol.*, 1934, *15*, 635–651.
9. FROSTBERG, N. Characteristic duodenal deformity in cases of different kinds of perivaterial enlargement of pancreas. *Acta radiol.*, 1938, *19*, 164–173.
10. GRAUER, F. W. Pancreatic carcinoma. *Arch. Int. Med.*, 1939, *63*, 884–898.
11. KAUER, J. T., and GLENN, F. Carcinoma of pancreas. *Arch. Surg.*, 1941, *42*, 141–155.
12. MACKINNON, D. C. Carcinoma of pancreas. *Minnesota Med.*, 1939, *22*, 281–283.
13. MILLER, J. R., BAGGENSTOSS, A. H., and COMFORT, M. W. Carcinoma of pancreas; effect of histological type and grade of malignancy on its behavior. *Cancer*, 1951, *4*, 233–241.
14. MILLER, E. M., and CLAGETT, O. T. Survival five years after radical pancreatoduodenectomy for carcinoma of head of pancreas. *Ann. Surg.*, 1951, *134*, 1013–1017.
15. MILLER, E. M., DOCKERTY, M. B., WOLLAEGER, E. E., and WAUGH, J. M. Carcinoma in region of papilla of Vater. *Surg., Gynec. & Obst.*, 1951, *92*, 172–182.
16. PAUL, L. W. Roentgen diagnosis of carcinoma of pancreas. *Am. J. Cancer*, 1936, *28*, 720–734.
17. POPPEL, M. H. Roentgen Manifestations of Pancreatic Disease. Charles C Thomas, Publisher, Springfield, Ill., 1951.
18. POPPEL, M. H., and MARSHAK, R. H. Roentgen diagnosis of pancreatic disease. AM. J. ROENTGENOL. & RAD. THERAPY, 1944, *52*, 307–316.

19. Ransom. Quoted by Berk.[1]
20. Rendich, R. A., Poppel, M. H., and Cove, A. M. Roentgen diagnosis of space-occupying lesions in region of head of pancreas. *Radiology*, 1942, *38*, 47–52.
21. Rigler, L. G. Diagnosis of extra-gastro-intestinal abdominal masses. *Radiology*, 1933, *21*, 229–237.
22. Rives, J. D., Romano, S. A., and Sandifer, F. M., Jr. Carcinoma of pancreas. *Surg., Gynec. & Obst.*, 1937, *65*, 164–177.
23. Weber, H. M., and Kirklin, B. R. Roentgenologic manifestations of tumors of small intestine. Am. J. Roentgenol. & Rad. Therapy, 1942, *47*, 243–253.
24. Whipple, A. O., Parsons, W. B., and Mullins, C. R. Treatment of carcinoma of ampulla of Vater. *Ann. Surg.*, 1935, *102*, 763–779.

DISCUSSION

Dr. James T. Case, Santa Barbara, California. This paper is a beautiful example of an orderly, well planned review and presentation of cases of a given pathologic lesion. Fortunately, the writers have had available for their study an unusually large series of cases of confirmed pancreatic carcinoma. They, themselves, call attention to one fault in this study, namely that a definite or suggestive diagnosis of carcinoma of the pancreas was made in a further large series which for various reasons did not come to biopsy or operative proof.

The high percentage of correct diagnoses or of suggestive findings sufficient to direct attention to a pancreatic lesion attests the value of the roentgen examination, as has been so well pointed out by the authors. For some reason, the idea seems to be general that enlargement of the curve formed by the sweep of the duodenum around the head of the pancreas should be a valuable sign in carcinoma of the head of the pancreas. My experience coincides with that of the authors—that this enlargement of the duodenal curve is much more likely to be found with pancreatic cyst or retroperitoneal tumors other than tumors of the pancreas. My first case recognized in 1913 was a somewhat fluctuating, right subchondral, palpable tumor. I reasoned that if it were a distended gallbladder, the duodenum would be displaced away from the liver; whereas if it were a tumor of the head of the pancreas, the duodenum would be displaced toward the liver. The latter condition obtained at the examination and I was able to make a correct diagnosis of pancreatic cyst. This case was reported in a paper presented before the American Gastro-Enterological Association in 1928.

The tabulation of dimensions of pancreatic carcinomas given by the authors makes it easy to understand why the spread of the duodenal curve around the head of the pancreas should not be anticipated in the majority of cases of carcinoma of the head of that organ.

Vol. 67, No. 4

# PSEUDOCYST OF THE PANCREAS ASSOCIATED WITH HYDROTHORAX*†

*By* ROBERT J. GROSS, M.D.,‡ ROBERT NULL, M.D., *and* WILLIAM LOEB, M.D.§
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THE mechanism involved in the association of benign intra-abdominal tumors with pleural effusion has been a provocative problem which still defies solution. Particular impetus was given to its study by the papers of Meigs[5] relating to the formation of ascites and hydrothorax with benign ovarian fibromas. The association of pleural effusion with malignant or inflammatory intra-abdominal disease is a well known phenomenon, the mechanism of which appears to be fairly well understood. Malignant involvement of the pleura may cause mechanical irritative, toxic or obstructive changes. Bacterial inflammatory involvement of the pleura causes formation of effusion by its direct effect on the blood vessels and lymphatic channels with changes in permeability. Among other common causes of hydrothorax are changes in the composition of the circulating blood such as hypoproteinemia, congestive changes with cardiovascular disease, intrathoracic tumors with vascular or lymphatic obstruction and traumatic injury to the chest. Much more puzzling is the elaboration of a theory which satisfactorily explains the formation of hydrothorax in the presence of benign intra-abdominal lesions. Although the formation of a hydrothorax with benign intrapelvic tumor in the female has become a fairly well known entity, an analogy to Meigs' syndrome has not been established in the male. The case presented touches on this problem in relation to the formation of a hydrothorax in association with a pseudocyst of the pancreas.

## CASE REPORT

D. M. This Negro male, aged twenty-seven, was admitted to the hospital in January, 1948, with a diagnosis of paranoid schizophrenia. During his entire hospital course there had been no change in his psychiatric status. On May 4, 1949, he was transferred to the medical service because he was unable to retain food, vomiting greenish colored fluid. He had apparently lost 15 pounds in weight from the time

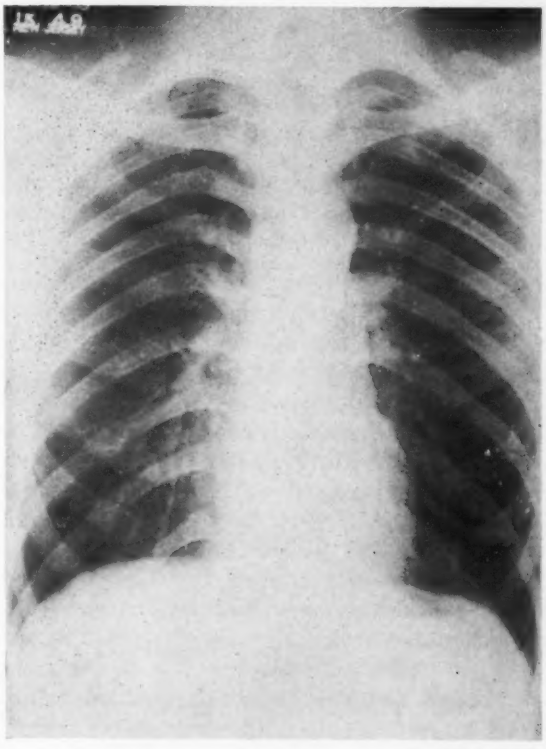

FIG. 1. Roentgenogram of the chest on May 15, 1949, showing no evidence of pulmonary or cardiac abnormality.

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† Reviewed by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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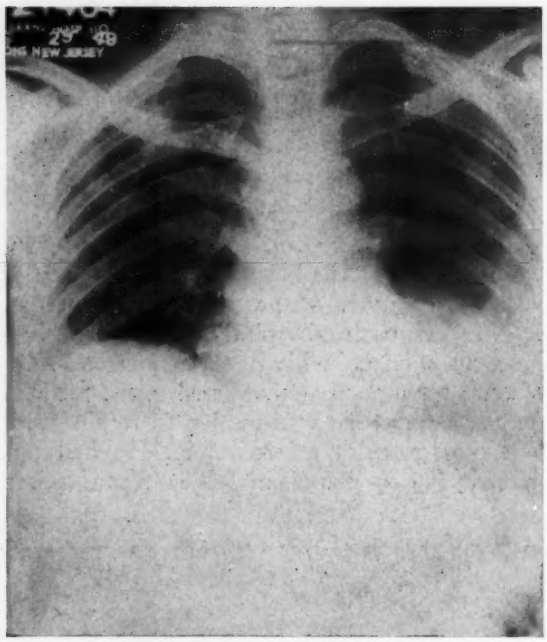

Fig. 2. Roentgenogram of the chest on June 29, 1949, showing pleural effusion at the left base obscuring parenchymal and diaphragm detail. A well defined, diffuse, dense clouding of the mid-abdomen is observed, which apparently depresses the transverse colon.

of admission to the time when his gastrointestinal disturbance was discovered. In the acute period immediately following the onset of his illness he lost approximately 20 more pounds. Physical examination revealed slight distention of the abdomen with rigidity. A chest examination at this time failed to reveal any evidence of abnormality (Fig. 1). Because of his mental condition he had to be tube fed, but despite this, the vomiting continued. The diagnosis was not clear and the patient was retained for further observation. He was first fed intravenously and then orally until a weight gain was noted. On June 27, he started vomiting again excessively, and his abdomen appeared distended. Temperature, pulse and respiration were normal. Physical examination at that time was reported to be essentially negative except for a doughy sensation in his distended abdomen with no marked or localized tenderness. Nasogastric drainage with Wangensteen suction and intravenous therapy was instituted. Two days later he was noted to have shifting abdominal dullness suggestive of abdominal fluid.

On June 29, a roentgenogram of the chest revealed dense clouding in the lower third of the left lung field obscuring the left costophrenic sinus and left leaf of the diaphragm, as well as underlying parenchmyal detail (Fig. 2). The laboratory data revealed a nonprotein nitrogen of 44 mg. per cent. Total protein was 6.23 grams per cent, sodium chloride 456 mg. per cent, carbon dioxide combining power 64 per cent. Urine examination was negative. The blood count was: 4,070,000 red blood cells; 13.5 grams of hemoglobin. There were 17,450 white blood cells, of which 85 per cent were neutrophils, 13 per cent lymphocytes, 2 per cent eosinophils. Stool studies were negative for blood, ova and parasites. On July 6, 700 cc. of straw-colored fluid was removed from the left chest. At this time a poorly defined mass was palpable in the left upper abdomen. This mass felt like a fluid-filled sac. Patient was maintained during this period almost completely on parenteral fluids and received 600,000 units of duracillin and 2 grams of dihydrostreptomycin daily. The streptomycin was administered because tuberculous peritonitis was suspected. On July 11, 1949, an abdominal para-

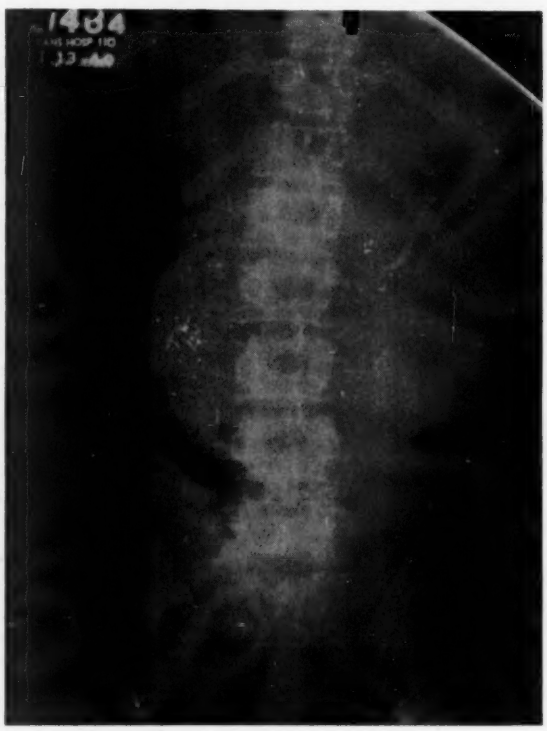

Fig. 3. Survey film of the abdomen showing well defined, dense, homogeneous clouding of the central and left portions of the abdomen depressing the transverse colon, associated with scattered dilated loops of small intestine with fluid levels.

centesis yielded 750 cc. of straw-colored fluid. Following this, the abdominal mass became more easily palpable and it felt more cystic than before. The abdomen became greatly distended and a Miller-Abbott tube was introduced but did not pass the pylorus. On successive days the left chest was tapped with removal of 900 cc. and 700 cc. of straw-colored fluid. On July 13, a survey film of the abdomen revealed a diffuse, dense, homogeneous clouding of the mid-abdomen, extending to the left lumbar and left hypochondriac regions and depressing the transverse colon. A few scattered loops of dilated small intestine containing fluid levels was observed (Fig. 3). A barium enema was attempted on July 18 and, although the colon was incompletely visualized, the film revealed a large, poorly circumscribed mass extending from the retroperitoneal area and pushing the transverse colon upward. A tube present in the stomach showed marked anterior displacement (Fig. 4). A transfusion was performed, and on July 19 exploratory laparotomy revealed a large retroperitoneal cyst which presented itself through the gastrocolic omentum with its base

Fig. 4. Lateral view of the abdomen following attempted barium enema showing anterior displacement of the transverse colon and a tube in the stomach by a large retroperitoneal mass.

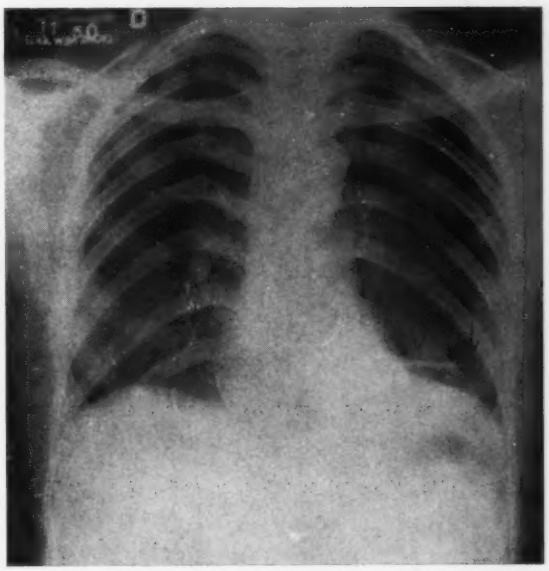

Fig. 5. Examination of the chest on January 17, 1950, showing marked increase in the space between the fundus of the stomach and left leaf of the diaphragm due to either subdiaphragmatic collection or encapsulated pleurodiaphragmatic effusion. This is associated with an area of atelectasis at the left base.

near the head of the pancreas. The cyst contained approximately 4 liters of milky white fluid. The cyst wall was marsupialized to the abdominal wall. Unfortunately, the fluid was not examined for the presence of enzymes. Histopathologic examination of the sac revealed a mesothelialized structure containing granulomatous areas as well as xanthoma and fat cells. Patient showed a remarkable degree of recovery thereafter with practically complete disappearance of the abdominal distention. A roentgenogram of the chest one month following operation showed no evidence of pleural effusion.

On one occasion the patient showed a reversal of the albumin-globulin ratio, namely, 3.7 grams of albumin, 4.1 grams globulin. This was treated with human serum albumin intravenously. On August 10, 1949, when the patient was ambulatory and the symptoms had completely subsided, roentgenographic examination of the fistulous tract was made utilizing iodochloral; this revealed a small pocket approximately 2 by 3 cm. in size. The evening following this examination the patient's temperature rose to 103° F. with a white blood cell count of 25,000; red blood cell count 3,780,000;

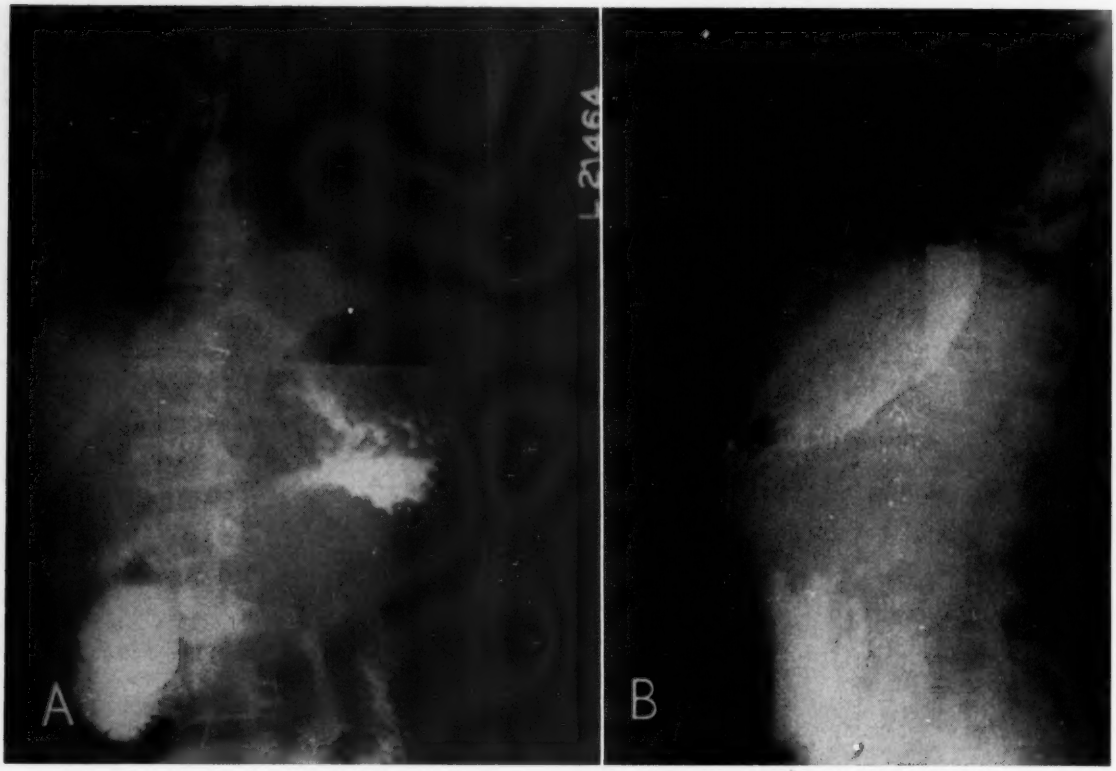


Fig. 6. (*A*) Barium study of the stomach showing evidence of extrinsic pressure on the greater curvature. Note the marked increase in the thickness in the space between the fundus of the stomach and the left leaf of the diaphragm. (*B*) Lateral study of the stomach following ingestion of barium showing anterior displacement of the distal end of the stomach and duodenal loop.

with 12 grams of hemoglobin. Chemotherapy was re-instituted, but his temperature remained elevated; he developed nausea and vomiting with recurrence of abdominal distention and tenderness in the right upper quadrant.

On August 16 there was a sudden spontaneous drainage of fluid from the fistulous tract. The symptoms then slowly subsided. Over the next few months the white blood cell count slowly returned to normal, the temperature returned to normal, but the cyst continued to fill and drain spontaneously.

On September 8, 1949, the fluid draining from the abdominal sinus was checked for enzymes. No evidence of pancreatic enzymes was detected. In October a barium enema examination was reported negative. On December 14, a chest roentgenogram was reported negative. The patient's abdomen again became progressively larger and a chest examination on January 17, 1950 (Fig. 5) revealed a marked increase in the thickening of the space between the fundus of the stomach and the left leaf of the diaphragm which was interpreted as either a subdiaphragmatic collection, or an encapsulated pleurodiaphragmatic effusion. Associated with this finding was a large area of plate-like atelectasis at the left base. A gastrointestinal series the same day (Fig. 6, *A* and *B*) revealed a large retroperitoneal mass which displaced the stomach upward and anteriorly. On January 18, 1950, a laparotomy was done and a pancreatic cyst was found. This was not apparently connected with the draining sinus tract. The cyst was anastomosed to the lesser curvature of the stomach. The postoperative course was uneventful and no further drainage occurred from the original sinus tract. Examination of the fluid from the cyst showed 33 mg. per cent of sugar, 240 mg. per cent amylase, and a specific gravity of 1.0177. Follow-up studies have shown no evidence of thoracic or abdominal fluid accumulation. A gastrointestinal series approximately a month after the second operation showed a normal gastrointestinal tract. The anastomosis site was not demonstrated.

DISCUSSION

Nora and Davison[6] described a series of cases of hydrothorax associated with intrapelvic tumor and, although most of the cases were due to ovarian fibroma, there were also cases of pseudomucinous cystadenoma of the ovary, uterine fibroid, and a fibroma of the left broad ligament. In the cases mentioned there seemed to be no relationship between the amount of ascites and the degree of hydrothorax.

Calmenson *et al.*[3] discuss certain pelvic tumors associated with ascites and hydrothorax and take up the theories which have been offered to explain the formation of chest fluid with an intrapelvic tumor. Among the factors they discuss are mechanical compression of the lymphatic channels, interference with the azygous system of venous drainage, as well as transperitoneal lymphatic passage of fluid or passage of an irritative substance from the abdomen into the pleural cavity. They also considered the "alarm reaction of Selye"as a possible mechanism in which the organism reacts to a damaging agent. Among the responses to "alarm" is the production of pleural and peritoneal transudates. One of the main stumbling blocks in the acceptance of these theories is that many other intrapelvic tumors similar in size, position and configuration do not cause these changes.

Relatively few cases have been reported in which the presence of a pleural effusion was noted in association with cysts of the pancreas. Alivisatos[1] described the case of a woman, aged twenty-six, whose abdomen became enlarged, causing edema of the leg and distention of the subcutaneous abdominal veins. She lost weight rapidly and suffered progressive dyspnea without pain. The dyspnea was due to a pleural effusion. Autopsy revealed a polycystic pancreas completely destroyed by cystic transformation except for 2 or 3 cc. of normal pancreatic tissue. The peritoneum was intact and Alivisatos postulates that the source of the fluid must have been the cysts rupturing into the abdomen. Histopathologic examination demonstrated the similarity of the fluid in the abodmen to that contained in the cysts. He believed that the fluid escaped into the pleural cavity via the diaphragmatic hiatus. The mechanism by which an inflammatory change in the pancreas can cause pleural effusion was described by Werner[11] who cited a case of chronic recurring pancreatitis and cholecystitis in which acute exacerbations of either of the diseases were associated with marked hemorrhagic pleural effusion on the corresponding side. Of considerable interest is the fact that the exudate contained large quantities of diastase which was much greater than the amount found in the blood. He postulated that the pancreatic secretion was carried through the lymph passages. The hemorrhage was attributed to the trypsin-vascular effect. Traquair[10] described a chylothorax following traumatic pseudocyst of the pancreas in a young male who was admitted two weeks after having been kicked in the epigastrium. At operation a pseudocyst of the pancreas was found which was drained externally. Five weeks later a left-sided pleural effusion developed which was chylous in character. In the discussion, Traquair mentioned that there was no chyle in the peritoneal effusion when the patient was first tapped. Therefore the chylous effusion was a late development and not a part of the original injury. He could not explain why it first appeared in the left pleural cavity and then afterwards in the peritoneal cavity. It was of interest that the draining of the peritoneal cavity had no effect on the pleural effusion. Phillips[8] described a male, aged twenty-two who had been kicked by a horse and developed some epigastric symptoms three weeks later. Five months following trauma he was admitted to the hospital with a markedly enlarged abdomen and signs of left pleural effusion. This was drained but the patient lost strength and died a month later. At postmortem enormous cysts of the surface of the pancreas were found. The greater omentum was adherent to the cysts

and to the duodenum and the stomach. The cyst contained approximately 3 liters of translucent greenish fluid. The percussion dullness did not change with the position of the patient during life and this was explained as due to adhesions. Pinkham,[9] in discussing the formation of pancreatic pseudocysts, stated that they usually form as a result of degenerative changes affecting the interstitial tissues of the gland or tissue adjacent to the pancreas when the corrosive action of the pancreatic ferments has led to an encapsulated accumulation about the gland. The cysts are usually found in one of three sites: between the stomach and the transverse colon under the gastrocolic omentum; between the stomach and the liver under the gastrohepatic omentum; or between the leaves of the mesocolon. However, some have been known to dissect retroperitoneally and present in the pelvis. There is no true epithelial lining, the pseudocyst being formed by dense connective tissue of variable thickness. Both true and false cysts may result from pancreatitis, possibly as a result of fibrosis constricting the duct with partial obstruction and dilatation distally, followed by degeneration of the acinar cells leading to necrosis of other tissues by action of the liberated ferments. Pinkham believes that the term "pseudocyst" should not be used since there is no definite way of differentiating hematogenic collections, pseudocysts, and pancreatic suppuration. Pascucci[7] gave a classification of the cysts of the pancreas and in his study of the literature found them to be very rare. He found no correlation between pancreatic lithiasis and cyst formation and thought it possible that the same initial pathologic condition (except trauma) is possibly the precursor of both cyst and stone. Jones[4] reported 2 cases of true pancreatic cysts which he described as being etiologically and morphologically similar to pseudocysts in that they contain blood, inflammatory exudate or small amounts of pancreatic fluid. Bickford[2] described 2 cases of traumatic pseudocysts of the pancreas with pleural effusion following closed abdominal thoracic injury. The effusion was on the left side in both cases and Bickford believed they were due to a concomitant injury to the chest wall or lung. He stated that he had been unable to find association of the left-sided pleural effusion with pseudocysts of the pancreas anywhere else in the literature.

## COMMENT

Hydrothorax associated with pseudocysts of the pancreas is apparently uncommon because search of the literature failed to reveal more than 6 cases in which an in flammatory component could be ruled out. The mechanism concerned with the passage of material from the abdomen to the pleural cavity by means of transdiaphragmatic lymphatics is well known and, of all the theories postulated, the most credible one appears to be that which explains the formation of the fluid as a result of either: (a) passage of an irritative substance (pancreatic ferment ?) through the diaphragmatic lymphatics to the pleural cavity where an irritative pleural effusion is set up, or (b) transperitoneal passage of ascitic fluid into the pleural cavity through the physiologic diaphragm openings.

## SUMMARY

A case of hydrothorax associated with pseudocyst of the pancreas is described. Some of the mechanisms involved in the formation of a pleural effusion in the presence of intra-abdominal tumor are discussed.

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## REFERENCES

1. Alivisatos, A. S. Pancreas polykstique. Kystes rompus dans l'abdomen et penetration due contenu dans la pelvre droite. *Bull. et mêm. Soc. méd. d hôp. de Par.*, 1920, *44*, 1181–1191.
2. Bickford, B. J. Traumatic pseudo-cyst of pancreas with pleural effusion. *Brit. M. J.*, 1948, *1*, 1134–1135.
3. Calmenson, M., Dockerty, M. B., and Bianco, J. J. Certain pelvic tumors associated

with ascites and hydrothorax. *Surg., Gynec. & Obst.*, 1947, *84*, 181–191.

4. Jones, E. S. Pancreatic cysts, with report of two unusual cases. *J. Indiana M. A.*, 1944, *37* 175–179.
5. Meigs, J. V. Tumors of the Female Pelvic Organs. The Macmillan Company, New York, 1934.
6. Nora, E. D., and Davison, R. M. Pleurisy with effusion associated with pseudomucinous cystadenoma; (Meigs' syndrome). *Dis. of Chest*, 1947, *13*, 423–435.
7. Pascucci, L. M. Pancreatic cyst and lithiasis. Am. J. Roentgenol. & Rad. Therapy, 1944, *52*, 80–87.
8. Phillips, S. Case of fatal pancreatic cyst of enormous size simulating ascites. *B. Clin. Soc. London*, 1901, *34*, 53–55.
9. Pinkham, R. D. Pancreatic collections (pseudocysts) following pancreatitis and pancreatic necrosis. *Surg., Gynec. & Obst.*, 1945, *80*, 225–235.
10. Traquair, K. Chylothorax following traumatic pseudocyst of pancreas. *Brit. J. Surg.*, 1946, *33*, 297–298.
11. Werner, H. Pankreatogene Pleuritis. *Zentralbl. f. inn. Med.*, 1942, *63*, 577–585.

# PRIMARY HODGKIN'S DISEASE OF THE STOMACH

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IN 1913, Schlagenhaufer[5] reported probably the first case of primary or isolated Hodgkin's disease of the stomach. Primary and secondary Hodgkin's disease of the alimentary tract is quite unusual. However, primary Hodgkin's disease of the stomach is very rare. A survey of the literature up to the writing of the paper by Pirkey and Roberts[4] brought to light about 22 cases. Symmers[6] has remarked that not a single instance of Hodgkin's disease of the gastrointestinal tract was found in 173 necropsies of patients having Hodgkin's disease, in five of the largest municipal hospitals in New York City.

Craver and Herrmann[2] state that about 15 per cent of the cases of Hodgkin's disease seen at Memorial Hospital develop gastrointestinal symptoms which are present at some time during the course of the illness.

A classification of Hodgkin's disease in which gastrointestinal symptoms are found, is as follows:

1. Intrinsic gastrointestinal lymphogranulomatosis, in which there may be either
   a. primary gastrointestinal lymphogranulomatosis, in which the disease is exclusively limited to the gastrointestinal tract, or
   b. secondary gastrointestinal lympho granulomatosis, in which the gastrointestinal tract is involved as a part of the generalized process.
2. Extrinsic gastrointestinal lymphogranulomatosis, in which the gastrointestinal symptoms are produced by disease extrinsic to the gastrointestinal tract.

The majority of patients with Hodgkin's disease primary in the stomach are in the fifth decade, and males predominate in the ratio of two to one.

Primary lymphogranulomatosis of the gastrointestinal tract may involve any part of the gastrointestinal tract. However, the stomach appears to be the most frequent site of involvement, and the pylorus is the portion of the stomach most frequently affected.

The symptomatology depends upon the portion of the digestive tract that is diseased. Thus, there may be signs of pyloric obstruction. Clinically, there may be symptoms that are not distinguishable from those of a peptic ulcer or a neoplasm. The clinical picture may present the following aspects:

1. An ulcer-like syndrome, with epigastric pain relieved in some instances by food or alkalies; postprandial distress, nausea, vomiting, gaseous eructations, anorexia, and hematemesis.
2. Weight loss of varying degree is present in most cases.
3. Other constitutional signs of Hodgkin's disease may be present, such as fever of the Pel-Ebstein type.
4. Moderate secondary anemia, leukopenia with increase in the transitional cells, eosinophils, and blood platelets may be present. However, there may be no significant change in the leukocyte count, except for occasional slight eosinophilia.
5. A palpable mass is uncommonly present.
6. Splenomegaly may be present; hepatomegaly is less often present.
7. Diarrhea, pruritus, skin pigmentation, jaundice, ascites, which are symptoms common to abdominal lymphogranulomatosis, may be present.
8. Superficial lymph glands may be enlarged; but they are infrequently so.
9. Gastric analysis may show achlorhydria; or the gastric acidity may be normal.

Macroscopically, the disease appears to be an infiltrating process with consequent thickening of the gastric wall. It may be

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limited to a small area or it may be diffuse, resembling linitis plastica. The lesion may be ulcerated, giving rise to hemorrhage or perforation. The adjacent lymph nodes may be large, discrete, and soft. The histopathology is that usually seen in Hodgkin's disease elsewhere. There is a great abundance of endothelial cells in all stages of transition to large mononuclear and multinuclear giant cells (Sternberg-Reed cells), plasma cells, and eosinophils.

The history and physical findings are of little value in the diagnosis. In the past, roentgenological diagnoses have been made preoperatively, but these cases are quite unusual. The only relatively constant finding is the presence of a lesion having a polypoid appearance, seen in the area of the infiltrated gastric wall. This roentgen finding should prompt the radiologist to keep in mind the possibility of Hodgkin's disease of the stomach.

According to Jungmann,[3] there are three types of Hodgkin's disease of the stomach: (1) an ulcerative type in which there are usually multiple flat ulcerations; (2) a tumor-like type, most frequently found in the prepyloric region of the stomach; (3) a type in which there are changes involving the whole stomach, described under the heading of polyposis of the stomach.

Gastroscopic examination has not been considered to be of any value in making the diagnosis of primary Hodgkin's disease of the stomach. As a matter of fact, it has probably been a detriment for any further treatment of these patients, since these examinations have tended to confirm the diagnosis of extensive carcinoma, thereby precluding further diagnostic procedures.

Bockus[1] states that a diagnosis of Hodgkin's disease of the stomach cannot be made except by histopathologic examination. He further adds that if the diagnosis of abdominal or glandular types of Hodgkin's disease is made by biopsy of an accessible lymph node in a case with roentgen and gastroscopic evidence of an infiltration in the stomach wall, malignant gastric lymphadenoma should be a diagnostic possibility. However, Hodgkin's disease of the stomach is so rare a condition that an independent gastric lesion would usually account for the gastric defects seen roentgenologically. Therefore, it appears that histopathology is the only certain diagnostic approach, and even then the differentiation from lymphosarcoma or lymphatic leukemia is often difficult.

The treatment for Hodgkin's disease localized to the stomach is gastric resection, followed by roentgen therapy. Curative results have been obtained quite consistently with this type of treatment.

## CASE REPORT

Mrs. A.C., aged fifty-two, was first admitted to the Mount Vernon Hospital, Mount Vernon, New York, August 10, 1949, complaining of pain in the mid-epigastrium. For approximately four months prior to her admission, she had been suffering from a continuous pain, which "felt like a brick in her stomach." The intensity of her distress was increased somewhat following meals. There was a 5 pound weight loss since the onset of the illness. The patient was a known diabetic for four years; however, she required no insulin, being maintained on diet.

On physical examination, no abnormalities were noted except for some muscle spasm and exquisite tenderness in the mid-epigastrium. No abdominal masses were palpable; nor were there any enlarged lymph nodes.

The laboratory data were as follows:

a. Hematological examination (August 10, 1949)

| | |
|---|---|
| Hemoglobin | 84%, 12.2 gm. (Sahli photoel.) |
| Color index | 1.0 |
| Red blood cells | 3,800,000 |
| White blood cells | 6,200 |
| Differential: | |
| Polymorphonuclear staff | 0% |
| Neutrophils | 72% |
| Eosinophils | 0% |
| Basophils | 0% |
| Lymphocytes | 26% |
| Monocytes | 2% |
| Platelets | Adequate |

Anisocytosis present

b. Urinalysis (August 11, 1949)

Negative for glucose; normal specific gravity; trace of albumin; 25–50 white blood cells; rare calcium oxalate crystals; few bacteria.

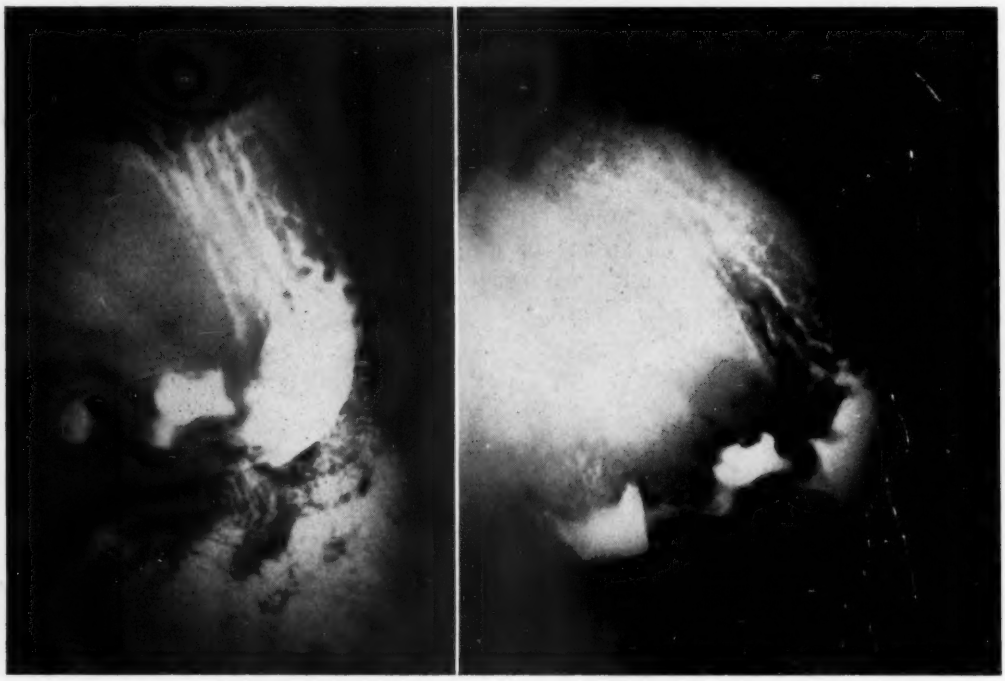

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Fig. 1 and 2. Polypoid filling defect involving the distal third of the stomach.

c. Blood chemistry (August 10, 1949)
Sugar.....132 mg. per cent (290 mg. per cent, Aug. 13)
Nonprotein nitrogen.....31 mg. per cent

d. Gastric analysis

| | Free HCl | Total Acid | Lactic Acid |
|---|---|---|---|
| F | None | 26° | None |
| 1 | 26 | 48 | None |
| 2 | 24 | 36 | None |
| 3 | 60 | 88 | None |
| 4 | 66 | 88 | None |
| 5 | 70 | 88 | None |

The roentgenographic examination, which included a gastrointestinal series, was performed prior to the patient's admission into the hospital. An infiltrating lesion on the posterior surface of the lesser curvature aspect of the stomach was demonstrated, and the roentgenographic impression was that of a polypoid filling defect involving the antral end of the stomach. In the differential diagnosis were included: carcinoma, benign tumor, *i.e.*, leiomyoma, benign hypertrophy of the gastric mucosa (Fig. 1 and 2).

A surgical consultation advised surgery; and, on August 15, 1949, a subtotal gastrectomy was performed. The liver, pancreas, large and small intestine were found to be normal. At the distal third of the stomach, along the lesser curvature aspect, a 3 by 4 inch ulceration was found, with a definite scar on the anterior gastric wall. The distal third of the stomach wall was thickened, while the remainder appeared normal. A 65 per cent gastric resection was done, including normal stomach well above the area of involvement. No lymph nodes were palpably enlarged.

Dr. George Sharnoff, Pathologist of the Mount Vernon Hospital, submitted the following pathological report:

Gross examination of a portion of stomach which measured 13.0 cm. in length revealed thickening of the wall, whose mucosa was somewhat hemorrhagic. A 1.0 cm. white nodular mass of firm consistency was noted in the midportion of the specimen. On the anterior wall of the lesser curvature, a deep ulcer crater was found. Further sectioning of the gastric mucosa showed several other nodular masses.

Microscopic sections through the area of ulceration showed a typical ulcer bed of granulation tissue with a thin layer of cellular debris. The circumscribed nodular masses described above revealed an invasion through the entire wall by diffuse sheets of large, somewhat pleomorphic mononuclear cells, with large, hyperchromatic, irregularly shaped nuclei.

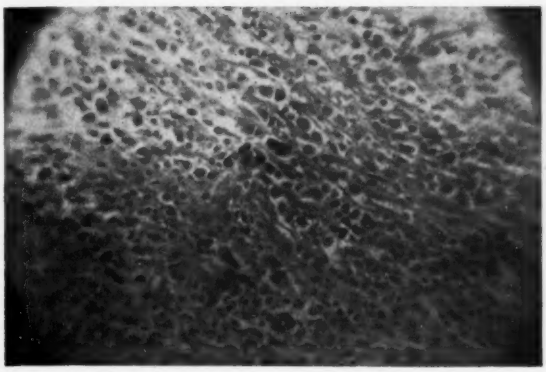

Fig. 3. Microscopic section showing the typical findings of Hodgkin's disease (courtesy Dr. George Sharnoff).

Numerous macronucleoli were present. There were occasional mitoses. Numerous lymphocytes, plasma cells and polymorphonuclear cells and occasional multinucleated giant cells (Sternberg-Reed character) were observed. Many of the polymorphonuclear cells were eosinophils. The histopathological diagnosis of Hodgkin's disease of the stomach was made (Fig. 3).

The patient's postoperative course was not remarkable, the procedure having been well tolerated. A course of postoperative roentgen therapy was decided upon, and was initiated on October 31, 1949. Two fields were used, including the left upper anterior and left upper posterior abdomen (20 by 20 cm.). A composite filter was employed, with rays generated by 200 kv. (peak), at a focal spot skin distance of 50 cm. The individual dosage was 300 r (air) to the field, with one field being treated every other day, for fourteen treatment days. Thus, the total dosage to each of the fields was 2,100 r (air). The patient tolerated the irradiation well. She was discharged after her last treatment on November 30, 1949, and was told to return to her own physician for follow-up.

The patient was returned to a private office of one of the authors (L.M.B.) for interval restudy of the gastrointestinal tract. The examination made on May 6, 1950, showed a normal enterostomy, and no recurrence of the tumor. The patient stated that she had been feeling well. She had lost approximately 20 pounds since the operative procedure. However, presently her weight is maintaining itself. Her diabetic condition is under control by dietary means, no insulin being required. She is now undergoing extensive dental work; twenty-one teeth have been extracted. Her physical examination is unrevealing except for the poor state of her dental hygiene. No lymphadenopathy is evident.

## SUMMARY

1. A brief outline of the literature concerning Hodgkin's disease, primary in the stomach, is given.

2. A case of localized Hodgkin's disease in the stomach is presented.

3. The clinical and roentgen features of the case, which we have reported, conform to those in the twenty-two cases which have already been reported in the literature.

4. However, the diagnosis finally rested upon the histopathological examination of the postoperative specimen.

5. The patient was given a course of roentgen therapy following operative intervention, and is now well a year following her hospitalization.

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## REFERENCES

1. Bockus, H. L. Gastro-Enterology. Sixth edition. Lea & Febiger, Philadelphia, 1947, p. 338.
2. Craver, L. F., and Herrmann, J. B. Abdominal lymphogranulomatosis. Am. J. Roentgenol. & Rad. Therapy, 1946, *55*, 165–172.
3. Jungmann, H. Hodgkin's disease of stomach. *Brit. J. Radiol.*, 1943, *16*, 386–387.
4. Pirkey, E. L., and Roberts, S. M. Diagnosis of primary Hodgkin's disease of stomach. *Radiology*, 1949, *52*, 75–78.
5. Schlagenhaufer, E. Ueber Granulomatosis des Magendarmtraks. *Zentralbl. f. path. Anat.*, 1913, *24*, 965.
6. Symmers, D. Clinical significance of pathological changes in Hodgkin's disease. *Am. J. M. Sc.*, 1924, *167*, 157–177; 313–339.

# AN EVALUATION OF INTRACARDIAC ANGIOCARDIOGRAPHY*†

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UTILIZATION of cardiac catheterization as a means of introducing a radiopaque medium into the heart was first employed by Egas Moniz *et al.*[3,5] in 1931. This procedure of intracardiac angiocardiography has been refined by Chavez, Dorbecker and Celis[2] and by Jönsson and collaborators,[4] and advocated as an improvement over the method of injecting the contrast material into a peripheral vein. The latter method of peripheral angiocardiography, introduced by Castellanos, Pereiras and Garcia[1] and by Robb and Steinberg,[7,8] occupies a position as a justifiable diagnostic procedure because of its simplicity and value in many types of cases. Satisfactory contrast visualization of certain structures, especially those of the left heart and aorta is, however, frequently difficult to obtain with peripheral angiocardiography. Efforts to improve upon the value of the entire procedure and to overcome such deficiencies inherent in peripheral injection of the contrast medium led to the previously mentioned investigations of Chavez and of Jönsson and also to the present undertaking. The purpose of this investigation was therefore to make a comparative evaluation of these two methods of angiocardiography, peripheral and intracardiac.

A critical analysis of the results obtained by the Preble Laboratory group at Cook County Hospital in a series of patients of many different types subjected to peripheral angiocardiography (Robb and Steinberg method) revealed that there was an appreciable number of cases in which satisfactory diagnostic roentgenograms were not obtained. The more frequently adults were examined and the greater the simplicity of the roentgen and film changing apparatus, the more often failures were encountered. Since the performance of diagnostic angiocardiography in both children and adults by means of relatively simple and inexpensive equipment has been a primary objective, the following analysis of cause of failure was necessitated.

Foremost among the causes was inadequate contrast of the particular vascular structure being examined with its surroundings. This lack of contrast was often due to interference of the various visualized structures with each other, since the contrast material is usually spread out through several portions of the heart and lesser circulation. At the time the aorta and left heart possessed maximum opacification, their contours were often obscured by a considerable amount of contrast material in the pulmonary vessels. Secondly, the concentration of the peripherally injected material did not become great enough in some cases to permit adequate contrast visualization of the desired structures. Numerous factors were responsible for decreasing the concentration: (1) dilution by blood from other veins while en route to the right heart; (2) transient pooling of the liquid in the arm and subclavian veins; (3) regurgitation of the substance into connecting veins due to the high pressure of injection; (4) spreading out of the medium so that its entrance into the heart chambers occurs over a period of seconds; and (5) occasionally, a slow injection due to a small arm vein.

Other difficulties and causes for failures have also been encountered. The accurate timing of the roentgen-ray exposures sub-

* From the Preble Laboratory of Northwestern Medical School and the Department of Roentgenology (Director, Dr. George Landau), Cook County Hospital, Chicago, Illinois. Read by title before the Central Society for Clinical Investigation, 1949.

† This investigation was aided by a grant from Mrs. Alfred Eustice. The 70 per cent diodrast used was supplied through the courtesy of the Medical Research Division of Winthrop-Stearns, Inc.

sequent to the injection of the contrast medium has frequently been difficult. This has been due to the great variability in the rate of flow of the medium to and through the heart chambers of different individuals. The fact that the material as a more dilute mixture spreads out through several structures at a time instead of remaining in a highly concentrated mass also contributes to the difficulty in timing the roentgen-ray exposures. Satisfactory positioning of the patient before the roentgen tube may be troublesome since the arm, with the cannula inserted into the antecubital vein, must remain straight. When the procedure was done in the supine position, it was occasionally impossible to place the patient properly for the desired view.

These difficulties of interference, low contrast in levoangiocardiograms, timing the exposure, and positioning the patient have combined to limit the value of peripheral angiocardiography. In many cases, especially in children, these limitations did not prevent making the correct diagnosis. The method failed to give the desired information, however, in over 35 per cent of adults with suspected lesions of the left heart and aorta. In the majority of individuals with thick, well muscled chests or concomitant lung infiltrations the resultant angiocardiograms lacked sufficient contrast. In general, lesions which were small and could easily be obscured by interference, necessitating sharp delineation, such as pulmonary stenosis and coarctation of the aorta, and lesions of the left heart, aorta and great vessels, including cardiac and major vessel aneurysms, have been difficult to visualize and this difficulty has been enhanced when these lesions occur in adults or heavy set individuals.

Direct intracardiac injection of the contrast medium has been advocated as a means of improving the diagnostic and experimental value of angiocardiography. The injection of the contrast medium as close to the lesion as possible offered two immediate theoretical improvements. It would increase the concentration of the contrast medium at the desired point by decreasing the dilution of the medium, and, secondly, it would eliminate structural interference with the levoangiocardiograms, since the material could be injected directly into the pulmonary artery or the right heart, thus avoiding visualization of the vena cava and right auricle. In order to obtain information as to the comparative value of this method, the group in Preble Laboratory used a procedure for direct intracardiac angiocardiography similar to that of Chavez, and we are indebted to his group for aid.

The technical procedure for direct intracardiac angiocardiography can be summarized as follows:

The patient was rejected if he had a definite allergic history or a positive reaction to either the conjunctival or intracutaneous test to diodrast. Auricular fibrillation was considered contradictory to the catheterization.

With the patient in the supine position, a pillow beneath his shoulders, head extended over the edge of the pillow, a branch of the right external jugular vein, as it passed over the sternocleidomastoid muscle, was selected by using the Valsalva maneuver. The vein was isolated under sterile surgical conditions through a small incision made under local anesthesia. After exposure, the distal portion was ligated, the vein nicked, and the catheter introduced into the lumen of the vein. The catheter used was the largest possible to introduce into the vein and was usually a 10, 12 or 14 F Levin tube, 35 cm. long, with an obliquely cut tip, liberally coated with vaseline. Saline was run through the catheter continuously after it had been introduced. The tip, as seen by roentgenoscopy or a control chest roentgenogram, which was routinely taken to establish correct exposure, was placed in the desired location in the right heart or pulmonary artery. Circulation time was determined by 50 cc. of saline containing 0.3 cc. of 2 per cent sodium cyanide solution injected in a fashion identical to that which is used for the subsequent injection of the contrast medium.[9] This circulation time method has been used in a large series of patients and has provided real aid in estimating the time of arrival of the contrast medium in the left heart.

After the patient was positioned on the roent-

gen table, 50 cc. of 70 per cent diodrast was injected manually through the catheter in less than one second. Roentgen-ray exposures were then made, one or two seconds after the beginning of the injection, for visualization of the right heart and pulmonary arteries if this was desired. For visualization of the left ventricle and aorta, subsequent exposures were made at a time equal to 10 to 20 per cent less than the sodium cyanide circulation time. The injection of diodrast was repeated after an interval of ten to fifteen minutes if different views, such as both anteroposterior and left anterior oblique, were necessary. Upon completion of the injections, the catheter was withdrawn, the wound closed with adhesive tape, and a small pressure bandage applied. The roentgen-ray exposure was made similar to that for bronchography. We have used a machine with a maximum output of 105 ma. at 100 kv. The cassettes of the Steleweld, Rayspeed (PB) type, with the grid built into them,* were moved manually beneath an inexpensive homemade table, shielded by lead, except for the space directly beneath the chest, and containing four or five cassettes.

This method of executing direct intracardiac angiocardiography has been used in a group of 36 patients with various types of cardiac, mediastinal and pulmonary lesions. A similar group of 47 patients has been subjected to peripheral angiocardiography. In a comparison of the performance and results of the two methods, the following *disadvantages* of the *direct intracardiac procedure* have become apparent:

1. *Technical performance.* The catheterization technique was more time consuming; at least five to ten minutes more are needed than for simple cannulation of an arm vein. The introduction of the catheter into the neck vein, advancing it into the heart, confirming the location of the tip in the desired position (right auricle in the majority of cases) required more time and mechanical manipulation than vein cannulation. In a few patients it was not possible to pass the catheter to the desired position; obstruction at the level of the clavicle was the most common. Nevertheless, injections made with the catheter only partially advanced still offered an improvement over the arm injections.

2. *Risk and reaction to the procedure.* In view of its possible sequelae it is presumed that intracardiac injection of the contrast medium involves a greater risk than peripheral injection. Chavez, Dorbecker and Celis[2] have reported 1 death in over 400 cases. In the present series there has been 1 fatality presumably due to the catheterization alone, prior to injection of the contrast medium, but the series is considered too small for a conclusion concerning the percentage of risk.

Transient cardiac arrhythmias were produced in about one-third of the patients subjected to intracardiac angiocardiography. The duration of the arrhythmias ranged from five to 180 seconds after the injection. Ventricular extrasystoles have been the most frequently encountered, while auricular fibrillation, short runs of nodal rhythm, and transient cardiac standstill have been encountered in a few cases. In every instance the original sinus rhythm was spontaneously restored.

The cause of these arrhythmias is at least three-fold: First, the mere contact of the catheter with the intraventricular septum or the atrioventricular valvular area produces irritation. Second, the rapid rate of the injection produces pressure elevation and thus irritation. A rapid injection of normal saline alone has been observed to produce arrhythmias. Third, the irritative effect of the iodine-containing contrast medium may be sufficient. Advancing the catheter tip only to the right auricle, as was done in most cases, avoids those cardiac areas most likely to produce serious arrhythmias with their attendant risk.[6]

The very rapid injection of the contrast material and small dilution of it made possible by the injection through the catheter is the key to the resulting excellent roentgenographic contrast. These same factors, however, were responsible for the more

* Furnished through the courtesy of the General Electric X-Ray Corporation.

sudden arrival of a more concentrated mixture of the medium in the visceral circulation. The resultant subjective reaction and frequency of nausea and vomiting was often more marked than is encountered with peripheral injection of the medium.

A final consideration of the aspect of risk involved concerns the increased opportunity for wound contamination. The introduction of a lubricated catheter into the vascular system through a neck vein demands a meticulous sterility, but the same care should be used in the cannulization of an arm vein. In the series reported there were no cases of infection.

In the actual routine performance of direct intracardiac procedure on over 50 cases, these disadvantages have been overshadowed. Two major advantages of this method over the peripheral injection were apparent in the studies on certain types of patients.

1. *Technical performance.* Once the catheter was introduced, the remaining portion of the technical aspect was greatly simplified. The patients walked about freely, positioned themselves before the fluororoentgenoscopic machine and the roentgen tube. The rate of injection of the contrast medium through the catheter is known from the circulation time determination (and from previous trials) and is invariable. The rate of injection is very rapid, usually less than one second through a 12 F catheter, and is dependent only on the operator. Errors in timing were far less frequent because of this. Positioning the patient on a horizontal table presented no problem or inconvenience for the patient or the individual injecting the dye. The frequency with which left anterior oblique views are desirable for best visualization of the aorta in patients with undiagnosed mediastinal lesions makes this ease of proper positioning important. These factors made the mechanical aspect of the injection a reliable and accurate affair. This substantially increased the ease and constancy with which satisfactory dextro- and levo-angiocardiograms could be obtained with a minimum of exposures and equipment. This carries with it the advantage of a smaller amount of radiation to the patient and the team than is encountered when many rapid exposures are made.

2. *Roentgenological results.* The closer the injection of the contrast material to the area to be studied, the better the resultant visualization of that area. Contrast visualization of the left heart and aorta in adults was substantially increased by rapidly injecting the medium into the right heart or pulmonary artery. This definite improvement in visualization of the heart and great vessels in a larger percentage of individuals is the most important advantage of intracardiac injection of the contrast medium. These results are in agreement with those previously reported by Chavez and by Jönsson. In some individuals the intracardiac method was the only way that satisfactory contrast and delineation of detail could be secured. The procedure may be diagnostic in such cases. Studies of cardiac function, of anatomical relationships, and of great vessel alterations can be made with greater accuracy in all cases.

A comparative summary of results obtained in two groups of individuals all over sixteen years of age, with similar types of cardiac, pulmonary and mediastinal lesions is presented in Table 1. Identical roentgen and film changing apparatus was used in both series. They are classified

Table I

CLASSIFICATION OF QUALITY OF LEVOANGIOCARDIOGRAM OBTAINED WITH INJECTION OF CONTRAST MEDIUM INTO ARM VEIN AND INTO SUPERIOR VENA CAVA OR RIGHT HEART VIA A CATHETER

| Group | Quality of Levo-angiocardiogram | Arm Injection 47 Cases | Catheter Injection 36 Cases |
|---|---|---|---|
| I | Not of diagnostic quality | 20 | 3 |
| II | Useful, but less than desirable contrast | 13 | 10 |
| III | Satisfactory contrast | 14 | 23 |

according to the quality of levoangiocardiograms obtained with the respective methods. Although the improvement may be due in part to the fact that technical and interpretive skill was greater due to experience at the time the majority of intracardiac injections were made, the figures in Table 1 illustrate the impression which the Preble Laboratory group had gained. The intracardiac procedure greatly enhanced the ability to produce satisfactory contrast visualization of the left heart, aorta and major vessels. This was of special aid in the differential diagnosis of vascular or non-vascular mediastinal lesions of adults. It is not the procedure of choice in infants and children in whom peripheral injection gives adequate results in most cases, nor in adults in whom right-sided visualization alone is adequate.

It is also of interest to examine the causes of failure in the two types of procedures. Incorrect timing of the films, in contrast to excessive diodrast dilution, was the cause of failure in one-third of peripheral angiocardiograms and in only 1 case of direct intracardiac injection. This observation illustrates the bearing which the intracardiac injection procedure has upon the worthwhileness and applicability of simple, manual film changing apparatus and low power roentgen equipment to angiocardiography. It has increased the potential value of such equipment. If the role of angiocardiography is that of widespread use, then the simple differential diagnosis of relatively common lesions, such as mediastinal masses in adults, by means of a minimum of equipment additional to standard hospital roentgen equipment, must become possible. The results of the present investigation indicate that direct intracardiac injection of the contrast medium can materially aid in this direction.

## SUMMARY

1. A comparison of two methods of performing angiocardiography, peripheral injection of the contrast medium and direct intracardiac injection via a catheter, has been made in a series of eighty-three cases.

2. The introduction of the catheter was more difficult and time consuming than cannulization of an arm vein. Positioning of the catheterized patient before the roentgen tube was more easily done, however, than with patients with a cannula in an arm vein.

3. Contrast visualization of the left heart and aorta of adults was materially improved by injection of the contrast medium into the heart. Several factors were held responsible for this: (a) higher concentration of the medium; (b) avoidance of interference of left heart and aortic shadows by right heart structures since the medium could be injected into the right ventricle or pulmonary artery; (c) increase in ease and accuracy in proper timing of the roentgen-ray exposures.

4. Direct intracardiac injection of the contrast medium proved to be a valuable procedure in the differential diagnosis of mediastinal or left heart structures in adults. The procedure increased the value and ease of use of low power roentgen-ray equipment and inexpensive film changing apparatus.

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## REFERENCES

1. Castellanos, A., Pereiras, R., and Garcia, A. La angio-cardiografía radio-opaca. *Arch. estud. clin. Habana*, September–October, 1937.
2. Chavez, I., Dorbecker, N., and Celis, A. Direct intracardiac angiography; its diagnostic value. *Am. Heart J.*, 1947, *33*, 560–593.
3. Egas Moniz, Lopo de Carvalho, and Almeida Lima. Angiopneumographie. *Presse méd.*, 1931, *39*, 996–999.
4. Jönsson, G., Bróden, B., and Karnell, J. Södersjukhuset, Stockholm. Personal communication.
5. Lopo de Carvalho, Egas Moniz, and Saldanha, A. La visibilité des vaisseaux pulmonaires (angiopneumographie). *J. de radiol. et d'électrol.*, 1932, *16*, 469–480.
6. Michel, J., Johnson, A. D., Bridges, W. C.,

Lehmann, J. H., Gray F., Field, L., and Green, D. M. Arrhythmias during intracardiac catheterization. *Circulation*, 1950, *2*, 240.

7. Robb, G. P., and Steinberg, I. Practical method of visualization of chambers of heart, pulmonary circulation, and great blood vessels in man. *J. Clin. Investigation*, 1938, *17*, 507.
8. Robb, G. P., and Steinberg, I. Visualization of chambers of heart, pulmonary circulation, and great blood vessels in man; practical method. Am. J. Roentgenol. & Rad. Therapy, 1939, *41*, 1–17.
9. Sutton, G. C., Wendel, G. E., Grant, H. E., and Warnick, E. G. Circulation times for angiography. Am. J. Roentgenol. & Rad. Therapy, 1950, *63*, 186–190.

# FOCAL MYOCARDIAL CALCIFICATION*

## REPORT OF A CASE

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MYOCARDIAL calcifications are rare. A case of calcification in a left ventricular aneurysm is presented.

J. M., a white American seaman, aged fifty-two, was admitted to the U. S. Marine Hospital, Staten Island, New York, January 9, 1950, for a repair of a right inguinal hernia. Past history revealed that he had led an active life as a seaman for thirty years, except for forty months between August, 1944, and January, 1948, when he was hospitalized at the Essex Sanatorium in Neptune, Massachusetts, for advanced pulmonary tuberculosis. Following treatment, the tuberculosis became inactive.

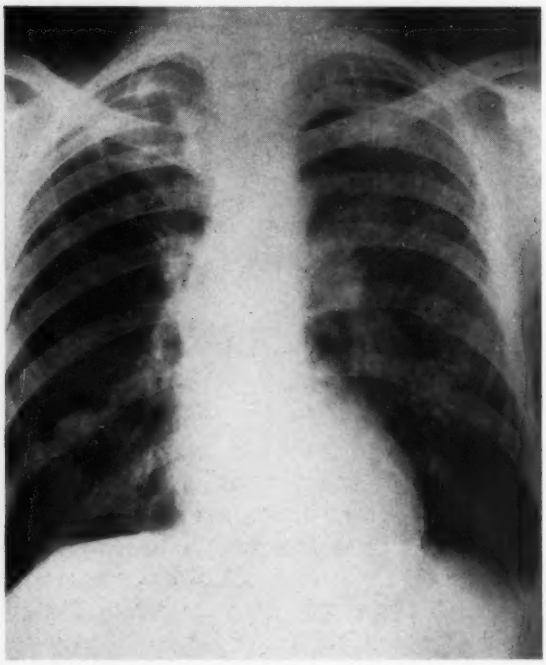

FIG. 1. Anteroposterior view, August, 1944, demonstrates evidence of far advanced fibrocaseous pulmonary tuberculosis with a large cavity in the right apex. A curved linear shadow of calcific density can be observed adjacent to the apex of the heart.

Upon admission he denied all symptoms referable to the chest and cardiac system. He had had no symptoms in the past suggesting myocardial infarction.

Physical examination showed, in addition to the right inguinal hernia, blood pressure 128/80, pulse rate 88, a trace of bilateral pedal edema, slight peripheral venous distention, normal sinus rhythm, and no cardiac murmurs.

The sputum was negative for acid fast bacilli. Serological tests for syphilis were negative. An electrocardiogram demonstrated a left bundle branch block (Fig. 7). The other laboratory tests were not remarkable.

A 70 mm. photofluorogram revealed calcification within the shadow of the left ventricle and an area of increased density within the right lower lung field. Roentgenoscopy revealed a crescentic, 6 cm. shadow of calcific density within the wall of the left ventricle near the

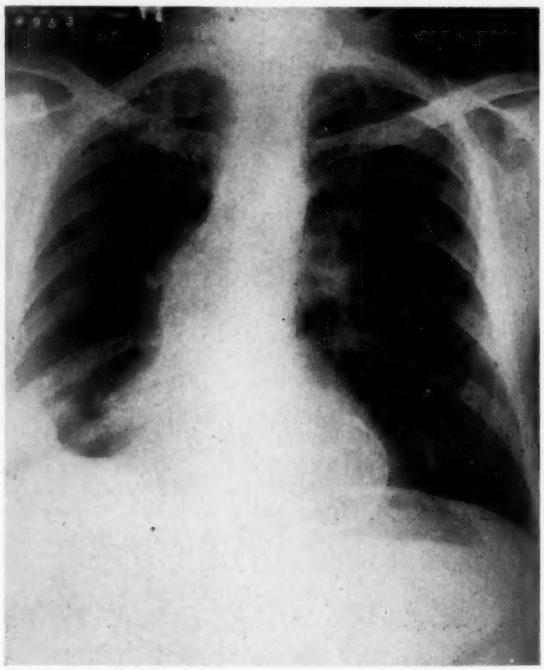

FIG. 2. Posteroanterior view, February, 1950, demonstrates extensive pleural thickening at the right base as residual of the pulmonary tuberculosis. A curved linear shadow of calcific density can be observed just inside the cardiac apex.

* From the Department of Radiology, U. S. Marine Hospital, Staten Island, New York (U. S. Public Health Service).

apex, and thickened pleura at the right base. The calcification moved with the heart beat but did not pulsate. The pulsations of the heart were recorded by kymography (Fig. 5). Comparison made with films taken in August, 1944, at Essex Sanatorium, Neptune (Fig. 1), shows that the calcification had not changed markedly in size during the six year period from 1944 to 1950. This is demonstrated in the present series of films in posteroanterior,

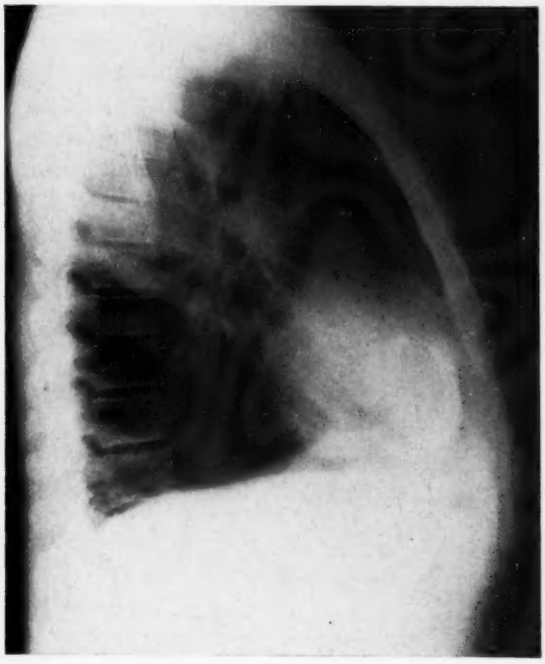

Fig. 3. Left lateral view shows the position of the calcification.

left lateral, and left anterior oblique projections (Fig. 2, 3, and 4). The far advanced pulmonary tuberculosis with cavitation was found to have regressed, leaving only evidence of residual pleural thickening at the right base. The roentgenographic diagnosis was: pleural thickening at the right base and focal myocardial calcification of the left ventricle.

The great majority of cardiac aneurysms are due to previous myocardial infarctions. The apex of the left ventricle is most frequently involved. Calcification in the wall of ventricular aneurysms is uncommon, but is of considerable value in the diagnosis of ventricular aneurysm.

Scholz, in 1924 was the first to describe

Fig. 4. Left anterior oblique view shows the hemispherical calcification within a bulge of the left ventricle.

a calcified ventricular aneurysm by roentgenographic examination during life.

Fig. 5. A kymographic record of pulsations about the calcified left ventricular aneurysm.

Fig. 6. Linear calcifications in the branches of the left coronary arteries in the region of the larger curved myocardial calcification.

Brean, Marks, Sosman and Schlesinger[2] reported 14 cases of myocardial infarction with calcification, and they stated that not more than 20 undoubted cases were in the medical literature. Bogoch and Christopherson[1] recently reported 2 cases.

Of the 14 cases reported by Brean *et al.*, 3 had no obtainable history of myocardial infarction. Three were entirely free of cardiac symptoms and they were able to do heavy manual work until shortly before death; however, 6 had severe angina.

On examination, 8 of their cases showed cardiac enlargement, and 8 had heart sounds described as diminished or of poor quality. Only one murmur was heard in the 14 cases. None of the patients had hypertension when seen. Only 11 of the 14 patients had an electrocardiogram made. Each of these showed evidence of myocardial damage: 6 had bundle branch block, 3 had auricular fibrillation, and 2 had paroxysmal ventricular tachycardia.

The positive history of tuberculosis and the total absence of coronary symptomatology, in the case presented, support the diagnosis of calcification of the pericardium rather than the diagnosis of calcification within a ventricular aneurysm. However, the oval bulging prominence along the left ventricular contour of the cardiac silhouette with the crescent of calcification within it, and the absence of pulsations in this area, except for those transmitted from the adjacent myocardium, substantiate the diagnosis of calcification within a ventricular aneurysm.

The differentiation of calcification within a ventricular aneurysm from extracardiac calcifications and the more common intracardiac calcifications of the pericardium, the myocardium, the valve rings, the valve leaflets, the coronary arteries, and the calcification of a cardiac tumor is best accomplished by roentgenoscopy. In roentgenoscopy, full dark adaptation of the eyes,

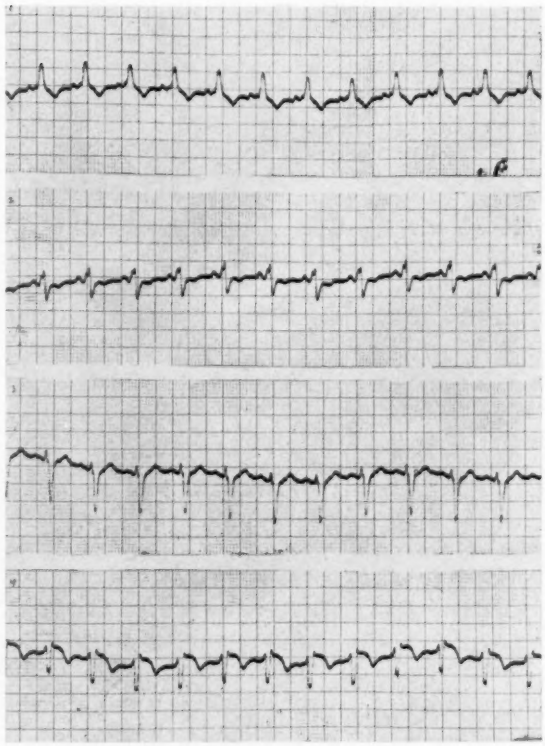

Fig. 7. Electrocardiogram reveals left bundle branch block.

the use of a fine focus roentgen tube, a fine grain screen, and a small aperture are essential. The technique for locating and identifying pericardial and intracardial calcifications has been well outlined by Sosman.[3]

In the case presented, the location of the calcification, its size and shape, allows it to be readily differentiated from the ring-shaped calcification of the mitral annulus fibrosus, the dancing nodular calcification of valve leaflets, and the linear calcifications of the coronary arteries (Fig. 6). Pericardial calcifications produce a thicker and more irregular shadow, and they are most frequently seen along the coronary sinus and around the right auricle and the right ventricle.

REFERENCES

1. Bogoch, A., and Christopherson, E. F. Calcified cardiac aneurysms. *Ann. Int. Med.*, 1950, *32*, 295–308.
2. Brean, H. P., Marks, J. H., Sosman, M. C., and Schlesinger, M. J. Massive calcification in infarcated myocardium. *Radiology*, 1950, *54*, 33–42.
3. Sosman, M. C. Technique for locating and identifying pericardial and intracardiac calcifications. Am. J. Roentgenol. & Rad. Therapy, 1943, *50*, 461–468.

# THE TREATMENT OF CARCINOMA OF THE SKIN*

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CARCINOMA of the skin is causing entirely too many deaths. In one recent year more than 3,000 persons in the United States died as a result of skin cancer.[4] The fundamental reason for such a shocking death rate is inadequate initial treatment. Other factors may, of course, enter in, including delay on the part of the patient, failure of the physician to recognize the condition, and the omission of biopsy. The fact remains that recurrence should not be permitted to appear, and our study has been directed toward a remedy for the failures.

Every radiologist probably sees many cases of recurrent carcinoma of the skin which were originally treated elsewhere, and few, if any, of his own. The patient's thought processes are largely responsible. Rarely does he recognize the seriousness of a skin cancer; he thinks of it as a simple complaint, and when it recurs after treatment he suspects incompetence on the part of the physician, and consults another.

We believe that recurrence of cutaneous carcinoma can be avoided. It is usually a deceptively simple condition to treat. Treatment must be custom-designed to suit the individual patient and the individual lesion. From a study of our own early cases which recurred and the many recurrences which we have observed in patients originally treated elsewhere, we have drawn up three fundamental rules which must be followed for successful control of cutaneous cancer.

*First*, performance of biopsy, without exception. Biopsy is absolutely essential, not only to ascertain the type of primary carcinoma, but many surface lesions are actually manifestations of metastases of deep-seated carcinomatous growths.

*Second*, complete excision of the growth when surgically treated. We have developed, in cooperation with our pathologist, a nearly fool-proof procedure for bisectioning of the excised mass to be sure that there is an uninterrupted margin of normal tissue surrounding the tumor.

*Third*, for radiation therapy, a calculation of the tissue dose for the *base* of the lesion, taking into consideration the total length of the treatment period. The treatments are given with care and complete knowledge of the agents employed. The necessity of including the entire tumor in the irradiated area is just as important as a complete excision.

In our clinic primary cutaneous carcinoma is the malignancy most often encountered. Of the 22,000 patients registered during the years 1932 to 1945, 6,502 were found by pathologic examinations to have some form of cancer, of which 1,204, or 20 per cent, had carcinoma of the skin. Our policy is to obtain a pathologic report on every initial lesion, but in some cases of multiple lesions the clinically obvious carcinomas were treated without repeated laboratory studies in order to spare the patient the additional expense.

Multiple primary lesions are frequently seen. Among the 1,204 skin cancer patients on whom pathologic examinations were made, 457, or 38 per cent, either had multiple lesions when first seen or later developed other primary carcinomas of the skin, and only those which were pathologically proved are included in this report. The number of cutaneous carcinomas varied from two to twenty-seven per patient; 50 patients, about 10 per cent of the group, each had more than ten lesions. A conservative estimate was made that a total of 3,800 separate carcinomas have developed in the 1,204 patients who were carefully studied in this series.

During the last twenty years, great

* Presented at the Thirty-second Annual Meeting, American Radium Society, New York, N. Y., May 25–26, 1950.

strides have been made in radiation therapy techniques. The actual tumor dose and the treatment period may now be calculated so that an adequate amount of radiation is delivered to destroy permanently a lesion of determined dimensions.[7,9,10]

Equal progress has been made in surgical techniques. For example, the sectioning and microscopic study of the specimen by the pathologist is indispensable in determining whether or not complete removal of the cutaneous growth has been accomplished.

The method of treatment is the choice of the physician, depending upon the characteristics of the individual case. In the following discussion, recent techniques and our present procedures are outlined in detail. The causes of local recurrence and failure which might lead to the death of the patient are emphasized. Since the problems of the treatment are similar, we will consider lesions in the epidermis which are metastatic as well as those which are primary.

## I. TYPES OF CARCINOMA OF THE SKIN

Cutaneous carcinoma is divided into two main types, the more common basal cell carcinoma, and the squamous cell carcinoma, according to which cells of the epidermis are involved. Mixed baso-squamous carcinomas are common, and clinical distinction between the three cannot be made without biopsy and microscopic examination.[5] Intra-epidermal carcinoma occurred infrequently and was the reason for several recurrent lesions. The discussion is not complete without considering secondary metastatic cancer of the skin, which may come from any malignant tumor, but most commonly from a primary cancer of the breast.

The basal cell carcinoma is by far the most common of the primary epitheliomas, accounting for 50 per cent of the cases. This lesion is locally invasive and malignant, but true metastasis does not occur.

The clinical appearance is usually a small, indurated nodule with a pearly appearance and the tendency to bleed with slight trauma. Certain basal cell carcinomas are cystic and are known as the adenocystic type. Growth is slow, and activity is usually indicated by the rolled, peripheral margin. Superficial epitheliomatosis, or multicentric basal cell carcinoma, is a special variety, with multiple foci or origin, and accounts for many recurrences when the condition has not been discovered by microscopic study of biopsy material. Occasionally basal cell carcinomas are pigmented, and not infrequently their appearance will simulate a melanoma. The true basal cell carcinoma is usually the most responsive of the primary lesions to irradiation, while the adenocystic type and the pigmented type are usually more resistant to radiotherapy.

Squamous cell carcinoma occurred in 30 per cent of the cases, and is not dependably distinguished from basal cell carcinoma by clinical examination. In the former, the history is usually of a shorter duration, ulceration takes place early, and metastasis occurs in a small percentage of cases. It may appear as a papillary outgrowth which quickly ulcerates; this ulcerative type is usually crateriform, with a minute crater and the typical rolled, indurated margin. The squamous cell carcinomas respond well to irradiation, although the optimum dose is somewhat larger than for a basal cell carcinoma.

Baso-squamous cell carcinoma occurred in 20 per cent of the cases, as determined by microscopic diagnosis. Clinically these tumors are indistinguishable from the true cell types, although their rate of growth may be more rapid, and the squamous cell elements are potentially capable of metastasis. The response to irradiation is the same as for plain basal cell carcinoma or squamous cell carcinoma. For all practical purposes, the total dosage is the same for all types, although we do find that lesions regress at a varying rate, and those that give the greatest concern are those which regress slowly.

Carcinoma may arise from the dermal

Fig. 1. Squamous cell carcinoma, Grade 2, arising in the epithelium of a sebaceous cyst. Such growths frequently remain unrecognized and are the cause of frequent recurrences.

appendages; basal cell or squamous cell carcinomas are an infrequent complication of a sebaceous cyst, and adenocarcinoma of sweat gland origin is occasionally reported. This group is successfully treated by surgical excision (Fig. 1).

Intra-epidermal carcinoma (Bowen's disease) is infrequent, and is correctly diagnosed only by microscopic examination. This condition is a frequent cause of so-called local recurrence, because it originates in multiple foci involving rather large skin areas. This condition is more common on the trunk and extremities, and our treatment is surgical excision with microscopic studies of the margins of the specimen to insure complete eradication.

The choice of treatment is based on two considerations: first, to effect a permanent cure, and second, to assure the patient the best cosmetic result consistent with a cure.

### 2. METASTATIC CANCER ON CUTANEOUS SURFACES

Secondary lesions reach the skin by direct invasion or through the lymphatics or blood vessels. The most common are metastatic lesions from a primary carcinoma of the breast. Primary cancer in almost any part of the body, however, may occasionally produce secondary foci.

A single cutaneous nodule is invariably treated by excision, and the widely removed specimen is utilized as a biopsy, as well as cure.

Multiple lesions, or those covering wide skin areas, are treated by irradiation. The majority of the cases are considered palliatively, and the over-all plan is based directly on the life expectancy of the patient: either a temporary control of the cutaneous lesions to avoid ulceration for a short time, or a more lasting control for a longer period of time.

The treatment is the same as for primary carcinoma and, in our experience, the single dose technique is often preferred for satisfactory palliation.

### 3. SURGERY

Early lesions of 1.0 cm. in diameter or less are almost always treated by surgical excision for biopsy and simultaneous cure. Since irradiation is not well tolerated over superficial bone or cartilage, epitheliomas on the hands, feet, legs (tibia), scalp, forehead and ears are usually excised. The cutaneous surfaces of the trunk are also treated in this manner, and other exceptions include lesions on the eyelid or face,

Fig. 2. Carcinoma arising on the skin of the chin in an area of radiation dermatitis.

regardless of size, where unnecessary deformity may result. Large lesions of 5.0 cm. or more in diameter, in any location, are usually treated by excision, with or without skin graft. Lesions of intermediate sizes are treated by surgery or irradiation according to the judgment of the therapist for the individual case (Fig. 2 and 3).

Prior to the excision of superficial cancer, local injection of 2 per cent procaine hydrochloride is administered as an anesthetic. A scalpel is used in preference to

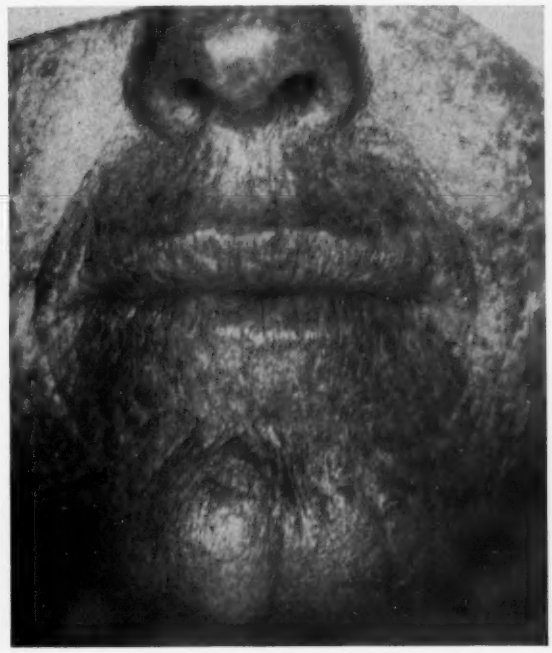

Fig. 3. The patient shown in Figure 2 fifteen years after a surgical excision and a plastic repair. Surgery is the preferred treatment of all lesions arising in areas of a radiation dermatitis.

electrosurgery to obtain a wound which heals promptly. The incision is carried at least 1.0 cm. beyond the visible and palpable margins of the tumor.

In our practice, early lesions are invariably removed in an elliptical fashion to provide a specimen which the pathologist can bisect transversely and diagnose by microscopic inspection, and at the same time report whether or not normal tissue exists around and beneath the growth. After excision, the cut surfaces are undermined and the skin edges drawn together

Fig. 4. Extensive basal cell carcinoma of the skin of the right cheek with a pathological report of multiple foci.

with or without subcutaneous reinforcement.

Large lesions are removed in a circular fashion, with most attention being given to the depth of the excision. In cases of

Fig. 5. The patient shown in Figure 4 seven years after a wide surgical excision and a plastic repair with skin graft.

clinical invasion of underlying cartilage or bone, as in the nose, ear, or scalp, the invaded structures are included in the specimen. Four or more specimens may be taken from the periphery of the lesion, if necessary, and examined by frozen section for the margin of safety of normal tissue. The majority of defects are closed immediately by split-thickness, full-thickness, or sliding skin grafts (Fig. 4 and 5).

In the series of 1,204 cutaneous carcinoma patients, surgery was employed in 583, or approximately 48 per cent; 268 cases were small lesions on which excision for biopsy and cure were performed. The remaining 315 cases were given a preliminary biopsy followed in a few days by local excision, and primary healing was accomplished on all except 33, which required skin graft. Three required amputation (2 of a finger, 1 of a leg). Of the small lesion group, the pathological report showed a wide margin of normal tissue in all but 34 cases; 11 of these wounds were re-excised during the following few days, the remaining 23 were treated by roentgen therapy or radium in sufficient doses to kill the remaining malignant cells.

Although we make every effort to follow up all of our cases and feel that this is extremely important, most of these patients do not realize the fundamental seriousness of their condition, and persistently ignore our communications so that the end result data are not complete; a summary of available data is given in Table III.

### 4. ROENTGEN THERAPY

The rationale of the radiation treatment of carcinoma of the skin is essentially destruction of the tumor cells. It is actually a radiation cauterization, although during the past few years we, and others, have considered the effect of protracting the period of irradiation for cutaneous lesions as for deep-seated malignancies, thus selectively doing greater damage to the physiology of the malignant cells than to that of the normal cells.[16]

The relationship of the total dose and the varying treatment period was experimentally shown first by Strandqvist[17] by his time-dose equation or his so-called isoeffect curve for plotting total dose with varying treatment periods.

Roentgen therapy has been employed satisfactorily over a range of from 50 to more than 200 kilovolts. Our experience has been largely with 100 kv. radiation, and in rare cases of deep invasion, 200 kv. has been used. Since there is apparently no proved relationship between the quality of the radiation used and the effectiveness of the treatment, the choice of technique is essentially geometric. Our choice of low voltage roentgen rays as the treatment for 265 cases, or 22 per cent of this series, ranging from early to far advanced lesions, was based on the optimum distribution of radiation for the particular lesion, considering the location, depth of involvement, period of treatment and cosmetic result. Our usual roentgen therapy technique utilizes 100 kv. (peak), 1 mm. Al added filtration, 5 milliamperes, 15.5 cm. target-skin distance; the latest calibration of output was 148 roentgens per minute, in air, with a half-value layer of 2.35 mm. Al. At a depth of 1 cm. the tissue dose is 60 to 70 per cent of the dose measured in air, depending upon field size.

The field of radiation is limited by a cone, lead shields, or both, with a margin of safety of 1.0 cm. around the visible and palpable margins of the lesions. The surrounding normal skin is protected by shielding it with 1 mm. of lead, which absorbs about 99 per cent of the radiation. Standard sizes and shapes are already cut, and this thin lead is easily cut and molded to fit the surfaces surrounding unusual lesions; 0.5 mm. lead foil will absorb more than 95 per cent of the radiation, and is frequently used for lesions with irregular contours. The lead-protective shield is held in place by adhesive plaster and by contact pressure from the various sized cones attached to the roentgen tube housing. The alignment of the axis of cylin-

drical cones must be very accurate, coinciding with the axis of the beam of radiation, since otherwise the irradiated field may not be the full circular field it is believed to be. There have been therapeutic failures due to this cause. The patient must be immobilized with sand bags and without pillows. The same therapist should give all the treatments.

Both the fractionation and the protraction of the total dose affect the biological response; small daily doses protracted over a long period produce less effect than a few large daily doses given within a few days. The total dose must therefore be higher if the treatment extends over a relatively long time.[6,8,12]

Since the exposure time for each treatment depends upon the intensity of the beam, measured in air, these doses are expressed in terms of roentgens, measured in air. However, the clinical criterion for the total dose is the actual tissue dose at the base of the lesion, calculated by Quimby's tables,[13] taking into consideration the total elapsed time over which the series of treatments is extended, in a manner similar to Strandqvist's findings.[1,17]

Fig. 6. Extensive baso-squamous carcinoma involving the entire surface of the left cheek. Invasion was considered to be at a depth of 1.0 cm. in different areas.

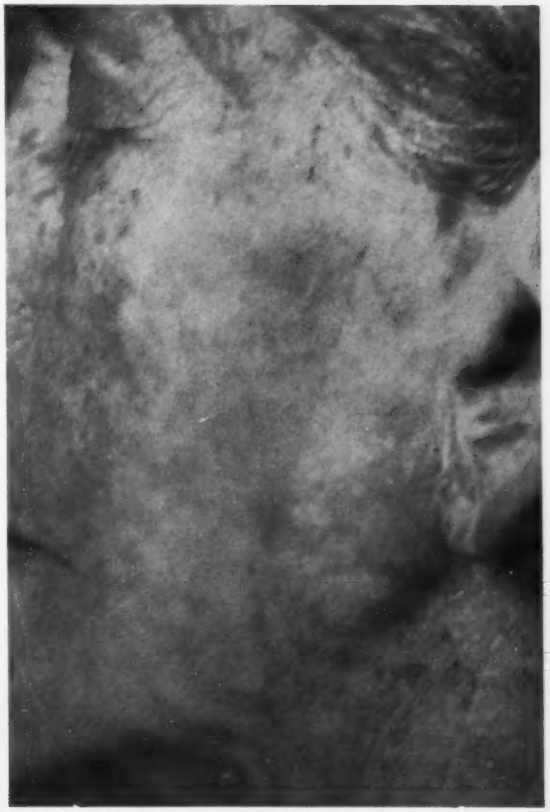

Fig. 7. The patient shown in Figure 6 following roentgen therapy in 1940. During a twelve day period the growth received 3,300 tumor tissue roentgens at a 1.0 cm. depth. A recurrence has not been observed for a ten year period.

*Single dose technique*, though not yet proved entirely satisfactory, may be used for small superficial lesions with a normal subcutaneous layer. Every safeguard for accuracy of application must be employed in single dose treatment. Underdosage runs the risk of recurrences; overdosage retards the recuperative power of the skin, producing an indolent ulcer with delayed healing, as well as a poor cosmetic result. Only lesions of 2.0 cm. diameter or less

have been given the single dose treatment, with the dosage ranging between 2,500 to 3,000 r, in air; at 0.3 cm. depth the tissue dose would be identical, 2,500 to 3,000 r.

The distance the patient had to travel and his occupational schedule prompted the occasional use of single treatment techniques, but in recent years we felt justified in insisting that he make arrangements so that the divided, protracted treatment can be given.

Palliation of multiple metastatic lesions is permissible by the single dose technique, however; such doses are usually 1,500 r, measured in air.

*Multiple dose technique* was used for the majority of our patients receiving roentgen therapy. Daily treatments were administered, extending from ten to twenty days, with the total treatment time dependent upon the daily dose. A protective shield including as nearly as possible a 1.0 cm. zone of normal skin around the lesion was used throughout the treatment. The daily dose varied from 350 to 500 r, in air, depending upon the size of the lesion, the structure of the underlying tissue, and the over-all treatment time planned[2] (Fig. 6 and 7).

The small lesions of 2.0 cm. diameter received 500 r, in air, daily for eight to ten treatments. Larger lesions were divided into two groups: those with a depth of invasion of more than 0.5 cm., and those that covered a relatively large surface but remained quite superficial. The first group of invasive tumors was treated by daily doses of 350 to 400 r, in air, for ten to fifteen treatments. In some cases, total doses were not decided upon until the end of the tenth treatment, because of individual variations in response. The large superficial lesions of the second group were treated in the same manner, with total doses, measured in air, 10 to 15 per cent less. Wide surgical excision and skin graft were used for more extensive lesions.

An important guide to daily and total dosage has recently been revealed in the description of the response of tumor cells to radiation.[16]

We did not use the Chaoul, or contact, roentgen therapy, though its usefulness in the treatment of *superficial* cancers is fully appreciated. The advantage of this method lies in the fact that the depth dose is very low; because the target-skin distance is less than 2 cm., the tumor proper receives the maximum exposure, and the underlying tissues receive a minimum of radiation.[3] In this form of therapy the single dose technique is applicable.

### 5. SURFACE RADIUM THERAPY

The recent trend toward various high and low voltage roentgen techniques should not entirely replace the flat surface radium applicator. Topical radium therapy offers ideal physical factors of irradiation to achieve a lethal tumor tissue dose with minimum damage to adjacent tissues. This modality was employed more frequently a number of years ago, but it still has definite advantages and was used for 312 patients, or 26 per cent of this series.[15]

When a radium source is close to the skin, the distribution of the radiation is such that the intensity falls off rapidly with increasing depth so that the underlying tissues are spared unnecessary irradiation. Spacing the radium source at a greater distance from the surface of the skin produces a distribution of radiation which does not decrease so rapidly with increasing depth, and hence is indicated for certain lesions with greater depth involvement; the exposure time must, of course, be appropriately increased.

The relative depth dose from a given radium applicator can be controlled, to a certain extent, by the proper spacing of the source from the surface of the growth. Assuming the dose at the surface of the cutaneous growth to be 100 per cent and neglecting absorption and scattering because they approximately cancel each other, the relative dose at any depth below the surface can be obtained from tables compiled by Quimby, and others.

These techniques provide us with methods of treating both the superficial and the more invasive cutaneous carcinomas. We

are able to create an intense radiation field in close proximity to the growth, and at the same time, due to the inverse-square law of diminution of intensity, the surrounding normal tissues are spared, both laterally and underlying.

In our clinic we use a minimum filtration of 0.5 mm. of platinum or 2.0 mm. of brass (equivalent) to absorb the beta radiation and obtain practically 100 per cent gamma radiation from the applicator.

The critical tissue dose, or tumor dose, is the exposure at the base of the growth. The lethal tumor dose of radiation delivered throughout the mass must be adequate to eradicate all of the diseased tissue. We have found that 4,000 to 4,200 gamma roentgens delivered in a single dose to the base of the lesion is adequate. The necessary exposures for our applicator are shown in Table II (Fig. 8 and 9).

A uniformly loaded, flat applicator is used for early and superficial lesions of the skin. Quimby's tables provide the best determination of the tissue dose obtained by the use of such an applicator. Such tissue doses were, until recently, expressed in terms of the biological unit, the threshold erythema dose.[9] Now, however, the gamma roentgen is properly defined and is in general use, and we have expressed our tissue doses from radium exposure in gamma roentgens. The doses quoted are in the center of the field, at the base of the lesion.

Fig. 8. A basal cell carcinoma of the right lower eyelid measuring 1.2 by 1.0 cm. in diameter with slight invasion of the subcutaneous tissues.

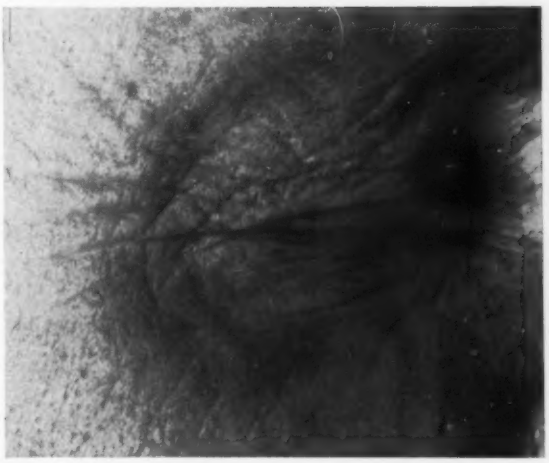

Fig. 9. The patient shown in Figure 8 eight years following surface radium therapy. In 1942, 3,800 gamma roentgens was delivered in a single dose at a depth of 0.3 cm. below the skin surface.

The oldest form of radium therapy is the application of radium with the applicator in contact; the distance from the source is then the thickness of the filter plus the radius of the radium unit.

Quimby's tables give the number of gamma roentgens per 100 milligram hours at various distances from uniform sources of various shapes. In the cases in this series, the axis of the radium cells (the actual source) was at 0.3 cm. from the surface. Consequently, the number of gamma

Table I

MILLIGRAM-HOURS REQUIRED FOR 4,000 GAMMA ROENTGENS AT VARIOUS DEPTHS BELOW THE SKIN

(Radium source at 0.3 cm. from external surface of flat applicator)

| Depth (cm.) | Plaque in Contact | Spaced 0.5 cm. | Spaced 1.0 cm. |
|---|---|---|---|
| 0.2 | 233 | 560 | 1,180 |
| 0.3 | 329 | 730 | 1,380 |
| 0.4 | 368 | 820 | 1,440 |
| 0.5 | 440 | 980 | 1,600 |
| — | — | — | — |
| 1.0 | 980 | 1,600 | 2,520 |

Fig. 10. An extensive basal cell carcinoma of fourteen years' duration which had invaded the right temporal area with invasion of the temporal fascia, the cartilage of the ear, and early invasion of both eyelids.

roentgens at 0.3 cm. from the source becomes the tissue dose value at the surface. The exposure from applicators of sizes and shapes and distances not given in Quimby's tables may be obtained by interpolation on a curve drawn through the tabulated values (Table 1).

(a) *Radium in Contact.* Early superficial growths with clinical evidence of not more than 0.3 cm. depth of invasion were frequently treated in this manner. In order to expedite this contact form of radiation, the bulky soft tissue overgrowth was in some cases first removed with an electric knife.

A single application of radium is usually sufficient. If the dose is adequate, therapeutic results are satisfactory and the chance of further tissue breakdown is less than with the divided dose technique. We used a small radium applicator, 1.5 by 1.0 cm., constructed with a wall thickness of 1.67 mm. of brass; the platinum filtration of the cells in addition made a total filtration of 2.0 mm. of brass, equivalent.

Our experience has proved the plaque-type applicator decidedly advantageous, especially when applied in contact with the surface of the growth and held accurately and closely by means of adhesive plaster. Further protection from undesired radiation on nearby surfaces, such as the eyes or other mucous membranes, or for shielding opposing surfaces, may be given by applying sheet lead to the side or top of the plaque.

The treatment is given in a single period

Fig. 11. The patient shown in Figure 10 eleven years following surface radium therapy. The treatment consisted of a surface application with a rectangular radium plaque with four treatment areas. The single dose technique was used and 4,050 gamma roentgens was delivered at 1.0 cm. depth. A recurrence has not developed.

ranging from eighteen to twenty-four hours, depending on the amount of radium used and the spacing. An average dose for early lesions is 4,000 gamma roentgens at a depth of 0.3 cm.; at 0.5 cm. depth the dose is 3,500 gamma roentgens, which would be inadequate for a thick lesion. The extent to which the underlying tissues are spared is shown by the fact that at 1.0 cm. below the surface, the dose was only 1,600 gamma roentgens. When a greater depth effect was indicated, the plaque was applied at some distance, or roentgen therapy was substituted (Fig. 10 and 11).

For the small group of lesions which cover a relatively large surface (up to 2.5 cm.) yet remain superficial, a long or rectangular applicator may be used effectively. The applicator we use for this purpose measures 2.5 by 1.0 cm., with two sets of eight to ten radium cells in the bottom, in tandem, in one layer. If the growth of cutaneous cancer is longer than the applicator, two applicators or multiple applications are used to cover the affected area. The dose for the single rectangular applicator was 500 mg. hr., which would give a tumor dose of 5,400 gamma roentgens at 0.3 cm. depth.

(b) *Radium Spaced.* When invasion of cutaneous tissue is more than 0.3 cm. in depth, either the radium applicator must be placed at some distance from the growth or roentgen therapy must be substituted. Under ideal conditions, irradiation is planned so that the entire growth receives a lethal dose with distribution as nearly uniform as possible. The distance between the applicator and the tumor may be regulated by a layer of cork or wood varying in thickness from 0.3 cm. to 1.0 cm. Opposing surfaces, in certain circumstances, must be protected by lead in addition to distance. In order to achieve the desired tissue dose at the base of the lesion, exposure in milligram hours must be proportionately increased when the applicator is spaced.

If the greatest diameter of a cutaneous lesion is less than 2.0 cm., a single applicator at a distance of 0.5 cm. for a dose of approximately 4,000 gamma roentgens to the base of the lesion is used. For growths involving a larger area, either the rectangular plaque is used or separate treatment areas are established and application and dosage given to each independently.

(c) *Interstitial Radium and Radon.* Interstitial radium therapy was used for 44 cases of cutaneous cancers in which the deeply infiltrated tumors were not in close proximity to bone or cartilage. Lesions, such as those on eyelids, which were near vulnerable structures were treated with radon seeds to minimize the exposure beyond the lesion. All might equally well have been given roentgen therapy, with appropriate shielding.

The use of interstitial radium needles is at times desirable. Their arrangement in and around a cutaneous tumor may produce quite uniform irradiation. Several different geometric systems have been developed and the tissue dose determined by appropriate charts for each plan (Paterson[12] or Quimby[13]).

We use both single and double needles. The single needles contain 2 mg. of radium and have an active length of 11 mm., with 0.5 mm. platinum walls.

Dosage is determined by the dimensions of the growth, irrespective of histopathology. In our limited number of cases, the tumor tissue dose ranged from 4,500 to 6,000 gamma roentgens, minimum. Needles with a length corresponding to the dimensions of the growth are selected. Injection of 2 per cent solution of procaine hydrochloride several centimeters from the margin of the growth eliminates discomfort and distortion of the tissues. The needles are inserted in a conical or cylindrical pattern and spaced approximately 1.0 cm. from each other around the peripheral margin of the cancer, and are sutured to normal skin (Fig. 12 and 13).

Radon seeds were used in cases of certain other lesions and in cases where recurrent growths invaded scar tissue. The total dose was similar to that of interstitial

Fig. 12. An extensive squamous cell carcinoma, Grade 3, of the right cheek with invasion to the buccal mucosa.

radium needles, with seeds of 1.5 to 2.0 mc. strength implanted at equal distance in the outer third of the growth.

### 6. Recurrent Cutaneous Carcinoma

The inadequacy of some prevalent methods of treating these lesions is emphasized by the appalling fact that 32 per cent of the group of 1,204 patients entering our clinic primarily because of carcinoma of the skin had recurrent lesions which had been treated elsewhere. Study of their histories reveals a common statement that a crust or ulcer had been present for varying lengths of time, and that the lesions had been treated by electrodesiccation, apparently disregarding the pathology involved.

Table 11 lists the methods used for the initial treatments elsewhere, in the order of the frequency of their use. At a glance, it is obvious that nearly every known method of destruction had been employed, but electrodesiccation was by far the most frequent method, probably because the equipment for this treatment is available in most physicians' offices; 45 per cent of the recurrent cases had been treated by electrodesiccation.

The proper uses for the electric needle have never been clearly defined, but the instrument is *not* indicated for cutaneous cancer. In a relatively smaller number, of recurrent cases, authentic types of treatment such as roentgen therapy (17 per cent), surgery (10 per cent), and radium (5 per cent), had been given inadequately,

Fig. 13. The patient shown in Figure 12 nine years following interstitial radium needle therapy. Radium needles were inserted in conical fashion around the ulcer and a dose of 6,200 gamma roentgens was delivered throughout the growth. A recurrence has not developed during this period.

due primarily to failure to obtain a biopsy. In other words, the treatments were not given for carcinoma but for benign lesions. The other forms of therapy shown in Table II were used on approximately 25 per cent of the recurrent cases, although they have no legitimate place in the treatment of cutaneous carcinoma (Table II).

The fact that stands out in the study of these cases is that only 9 patients, less than 3 per cent, were given preliminary biopsy and a microscopic diagnosis. Pathological reports, had they been made, would undoubtedly have excluded all forms of treatment except surgery, roentgen therapy, or radium. In the presence of a positive diagnosis, the standard forms of therapy would undoubtedly have reduced the incidence of recurrence of cutaneous cancer from 30 per cent to less than 10 per cent. Local recurrences, or new lesions near the scar of pathologically proved cancer due to multiple foci or Bowen's disease, have been discussed.

The treatment recommended for recurrent cutaneous carcinoma should be the one giving the surest curative and best cosmetic results. The therapist should understand not only the peculiarities of the various cellular types, but also the physical and practical application of the various forms of radiation as well as the surgical techniques. Our treatment for recurrent cutaneous carcinoma is predominantly surgical excision and, if necessary, plastic repair. To prove the complete excision, the tissue specimen should be examined microscopically, and a margin of safety of normal tissue both around and beneath the growth should be obtained. If incomplete, further excision is indicated or radiation therapy is instituted as though only a biopsy had been done. Study of our earlier cases which did not have the benefit of this analysis of the resected mass leads us to conclude that recurrent carcinoma originates from malignant cells more or less incorporated in scar tissue, which indicates surgical rather than irradiation procedures.

TABLE II

RECURRENT CANCER

| Previous Treatment | Number of Cases | Treatment Prescribed | | |
|---|---|---|---|---|
| | | Surgery | Radium | Roentgen Therapy |
| Desiccation, cautery, curettage | 173 | 74 | 62 | 37 |
| Roentgen therapy | 72 | 45 | 17 | 10 |
| Surgery, scalpel | 42 | 16 | 21 | 5 |
| Acid, caustics, iodine | 28 | 14 | 7 | 7 |
| Radium | 21 | 19 | 1 | 1 |
| Zinc-sulpha., carbolic, podophylin | 16 | 5 | 7 | 4 |
| Carbon dioxide | 16 | 7 | 3 | 6 |
| Actinic ray, Ultraviolet | 9 | 6 | 3 | — |
| Unknown | 7 | 4 | 2 | 1 |
| Total | 384 | 190 | 123 | 71 |

### 7. PROGNOSIS

The cure of cutaneous carcinoma may be attained equally well by surgery, radium, or roentgen therapy, but cosmetic results are most satisfactory with irradiation. In general, recurrent lesions develop in approximately the same percentages for each modality. We consider as recurrent the reappearance of disease within 1.0 cm. of the margin of the scar during the five year period. The type of cases likely to be recurrent are those with a primary growth and area of skin around it which is hyperkeratotic which may actually demonstrate multiple microscopic carcinomatous foci or multiple lesions. In retrospect, we believe that if such entire areas were treated as carcinomatous, our recurrences might well be reduced one-half. Over the period from

Table III

FIVE YEAR END RESULTS FOR THE INITIAL CUTANEOUS CARCINOMA

(79 per cent follow-up on 1,204 patients)

| | No. of Cases Followed | Free of Recurrences | No. of Recurrences | Percentage Recurrences |
|---|---|---|---|---|
| Surgery | 475 | 408 | 67 | 14 |
| Roentgen therapy | 219 | 195 | 24 | 10 |
| Radium | 289 | 271 | 18 | 17 |
| Total | 983 | 874 | 109 | 11 |

1932 to 1944, 79 per cent of the patients entering our institution primarily for cutaneous carcinoma were followed for that lesion for a five year period or longer. As shown in Table III recurrences developed in 11 per cent of the patients who were followed. The incidence of recurrence was somewhat higher for surgery than from radium or roentgen therapy. Practically all of our recurrent growths were treated by surgery.

Regional or distant metastatic involvement was present or developed in 16 out of 1,204 patients, or 1.3 per cent, and radical surgery is the procedure of choice for all operable regional metastatic node areas.

In this series, 7 patients died from cutaneous carcinoma; 6 were recurrent from three to twenty-two times, and 5 had the disease for over ten years. Palliative therapy only could be given to 3 of the patients, surgery for 1, and roentgen therapy for 2 patients. The remaining 4 patients received curative therapy by one or a combination of the three modalities. They ultimately died from their disease, a mortality rate of 0.58 per cent.

SUMMARY

1. A biopsy and pathologic diagnosis is the initial procedure for the treatment of cutaneous carcinoma.

2. Early treatment by surgery, roentgen rays, or radium is important for a successful result.

3. The first therapeutic effort should be the last.

4. From the analysis of our patients, the choice of treatment is an individual problem, and the selection between the three modalities is based on the anatomical areas, size of the lesions, tissue states about the growth (scar tissue, infection), and the adaptability of the patient for the selected therapy. Surgery is selected for certain lesions on the principle of excision for biopsy and cure, and for other lesions where irradiation is contraindicated.

5. Roentgen therapy by protraction and fractionation with 100 kilovolt equipment proved our best irradiation method; the treatments are planned on the time-dose relationship.

6. Radium therapy by topical application is frequently selected for early lesions, and interstitial therapy is effective for the deep invasive lesions where surgery may be contraindicated.

7. On the basis of our five year follow-up, a recurrence rate of 11 per cent and a mortality rate of 0.58 per cent was found.

We wish to acknowledge the valuable assistance given us by Robert E. Pugh, physicist (D.A.B.R.).

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REFERENCES

1. Ahlbom, H. Points regarding "time factor" in roentgen irradiation with divided dosage. *Acta radiol.*, 1946, *27*, 223–227.
2. Baclesse, F., Dollfus, M. A., Ennuyer, A., and Reverdy, J. La radiothérapie des épithéliomas des paupières. *J. radiol. et d'électrol.*, 1946, *27*, 515–526.
3. Breed, J. E. Beta-ray treatment of diseases of eye and its appendages. Prepared for an exhibit at American Radium Society meeting, Atlantic City, June 5, 1949.
4. Cancer mortality in the United States. National Office of Vital Statistics, December, 1949, Vol. *32*, No. 1.
5. Eberhard, T. P. Treatment of epitheliomas of skin. *Radiology*, 1947, *49*, 620–626.
6. Hale, C. H., and Holmes, G. W. Carcinoma of

skin; influence of dosage on success of treatment. *Radiology*, 1947, *48*, 563–569.

7. Hunt, H. B. Cancer of eyelid treated by radiation, with consideration of irradiation cataract. Am. J. Roentgenol. & Rad. Therapy, 1947, *57*, 160–180.
8. Martin, C. L. Time factor in radiation therapy. Am. J. Roentgenol. & Rad. Therapy, 1948, *59*, 1–8.
9. Martin, H. E. Quimby, Edith, H., and Pack, G. T. Calculations of tissue dosage in radiation therapy. Am. J. Roentgenol. & Rad. Therapy, 1931, *25*, 490–506.
10. Miescher, G. Recent experiences in field of radiotherapy in skin cancer. *Radiol. clin.*, 1947, *16*, 343–378.
11. Pack, G. T. Treatment of cutaneous epithelioma *Arch. Dermat. & Spyh.*, 1946, *53*, 576–585.
12. Paterson, R. The Treatment of Malignant Disease by Radium and X-Rays. Williams & Wilkins Company, Baltimore, 1948, pp. 206–237.
13. Quimby, Edith H. History of dosimetry in roentgen therapy. Am. J. Roentgenol. & Rad. Therapy, 1945, *54*, 688–703.
14. Quimby, Edith H. Dosage calculations in radium therapy; (exhibit). Am. J. Roentgenol. & & Rad. Therapy, 1947, *57*, 622–627.
15. Sharp, G. S. Treatment of cancer of eyelids. *J.A.M.A.*, 1938, *111*, 1617–1622.
16. Smithers, D. W. The X-Ray Treatment of Accessible Cancer. William Wood & Company, Baltimore, 1946.
17. Strandqvist, M. Studien über die kumulative Wirkung der Röntgenstrahlen bei Fraktionierung; Erfahrungen aus dem Radiumhemmet an 280 Haut- und Lippenkarzinomen. *Acta radiol.*, 1944, Supp. 55, pp. 1–318.

# MORTALITY IN SWINE AND DOSE DISTRIBUTION STUDIES IN PHANTOMS EXPOSED TO SUPER-VOLTAGE ROENTGEN RADIATION*†

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## INTRODUCTION

BECAUSE swine fall within the same radiosensitivity range as that estimated for man and because they can be selected to closely approach the weight and body thickness of man, they are suitable for many types of experiments dealing with the effects of total body irradiation. At the Bikini atomic bomb tests in 1946 they were among the experimental animals placed on the target ships. Subsequent study has provided useful information about the lesions produced by large doses of ionizing radiation from an atomic source.[3,4,6,7,8] It was desired to elaborate our knowledge of the pathology of acute total body ionizing radiation injuries because of the scientific interest and military implications of the syndrome. Under controlled laboratory conditions using a 1,000 kv. (peak), 3 ma. roentgen-ray source at 1 meter target skin distance, we found that the 50 per cent lethal dose in 30 days ($LD_{50/30}$) for 110 to 240 pound swine was approximately 275 r delivered to each lateral aspect of the animal for a total dose of 550 r.[9]

Since depth dose measurements indicated that the 1,000 kv. (peak) generator delivered 50 per cent of the air dose to about the median sagittal plane of the swine, one-half of the total dose was given to each lateral aspect in order to achieve more uniform distribution throughout the swine. As uniform a dose distribution as possible was desirable in order to more nearly approximate the results produced by the high energy atomic sources at Bikini.

The importance of considering the dose distribution factor in large animal roentgen irradiation studies was evident. For instance, a 600 r air dose given to each lateral aspect of swine for a total dose of 1,200 r produced 100 per cent mortality.[9] However, 2 out of a total of 4 animals exposed were able to survive 1,200 r when the dose was delivered to only one lateral aspect. One survivor was exposed on the left lateral aspect and 1 on the right. Thus, it seemed apparent that although the total dose delivered was the same by the two methods of exposure, the difference in the distribution of the dose altered the ability of the swine to survive the 1,200 r.

In order to further elucidate the importance of the dose distribution factor in total body roentgen irradiation of large swine, experiments were designed to compare the effect of unilateral and bilateral exposures to a 2,000 kv. (peak) source.

## MATERIALS AND METHODS

*Physical.* The radial beam of a 2,000 kv. (peak), G.E. Industrial X-ray Machine was used to irradiate swine, as shown in Figure 1. A relatively uniform field for exposing 8 large swine at one time was found at a distance of 2 meters from the tube in that portion of the beam between 95 and 103 degrees from vertical (Fig. 2). The output at this distance was 15 r/min $\pm$ 2 per cent.

A detailed discussion of the physical characteristics of the machine has been published elsewhere.[2] Pertinent physical data for this experiment are as follows:

| | |
|---|---|
| Kv. (peak) | 2,000 |
| Ma. | 1.50 |
| Target skin distance | 2 meters |
| Inherent filter | 6.3 mm. Fe |
| Added filter | none |
| Useful field | 50,000 cm.$^2$ |
| Half-value layer | 4.3 mm. Pb |

* From the Naval Medical Research Institute and the Bureau of Animal Industry, United States Department of Agriculture.

† The opinions are those of the authors and do not necessarily reflect the official views of the Navy Department or the Department of Agriculture.

From measurements in a masonite phantom the following average depth doses were obtained:

| Depth in cm. | Per cent of r delivered in air |
|---|---|
| 0 | 116.0 |
| 3 | 108.1 |
| 7 | 91.0 |
| 11 | 73.3 |
| 15 | 56.4 |
| 20.7 | 41.5 |
| 28.3 | 26.1 |

Following a warm-up period, the machine was calibrated with a 100 r Victoreen ionization chamber before each exposure. The output of the machine remained constant in an arc of 360° around the tube during the time the experiments were in progress. The exposure times for individual experiments varied from thirteen to fifty-four minutes depending on the size of the dose of radiation.

The exposure cages were built of plywood sides which contained numerous 3 inch airholes and $\frac{3}{4}$ inch dowel holes. The ends were $\frac{3}{4}$ inch pine hinged at the bottom and secured with a hasp at the top. The top, the floor, the corners and the base were of sturdy reenforced wood construction. The cages were curved, forming an arc of a circle with a 2 meter radius (Fig. 1 and 2).

During the exposure period the animals were held in place with through-and-through $\frac{3}{4}$ inch maple dowels inserted in the cage to conform roughly to the body outline of the swine. Small individual fans were provided to maintain good ventilation within the cages.

At the mid-point of each given dose in most of the experiments, 4 of the 8 swine were reversed in their cages so that they received half of the given dose on each lateral aspect while the remaining 4 swine received the entire dose on one lateral aspect (about half the animals on the right lateral aspect and the others on the left). We refer to the former as the bilateral or divided dose and indicate it as, *e.g.*, 200 r/2, while the latter is called unilateral or single dose and is indicated as, *e.g.*, 200 r/1. In both of the two examples given, 200 r is the total dose delivered to the swine. Five to ten minutes were required to reverse the animals in their cages.

*Animals.* The swine were obtained from the Animal Husbandry Experiment Station, Bureau of Animal Industry, Agricultural Research Center, United States Department of Agriculture, Beltsville, Maryland, where they were farrowed, raised and held until the morning of their use in the experiments. They were transported 8 at a time by truck to the Naval Ordnance Laboratory, White Oak, Maryland, for irradiation, following which they were taken to the animal runs at the Naval Medical Research Institute, Bethesda, Maryland, for observation and study. The animals were well nourished barrows of Landrace-cross breeds. Many were litter mates. At the time of roentgen irradiation they were $4\frac{1}{2}$ to $6\frac{1}{2}$ months old and weighed an average of 136 pounds. The smallest animal weighed 113 pounds, the largest, 161. Three of the swine weighed 113 to 119 pounds, 25 weighed 120 to 129 pounds, 49 weighed 130 to 139 pounds, 26 weighed 140 to 149 pounds, 9 weighed 150 to 159 pounds, and 3 weighed 160 to 161 pounds. In view of the fact that all were irradiated in the prone position in such a manner that the sides of the animal touched the sides of the rigid cage, the animals can be considered to have roughly the same thickness of body, namely, the width of the cage or 28 cm. (Fig. 2).

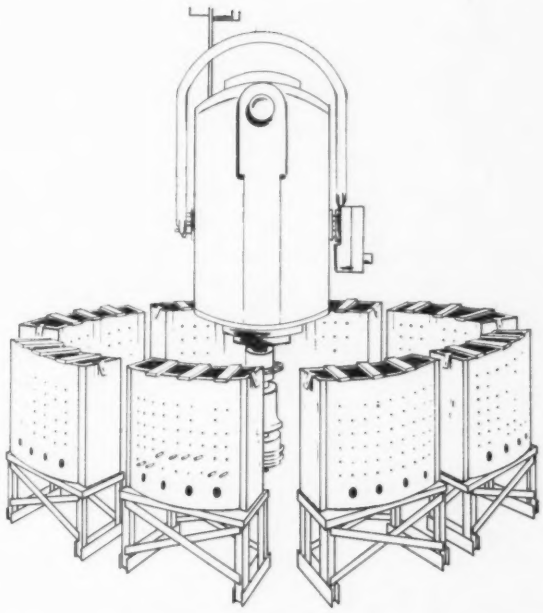

Fig. 1. Two thousand kilovolt roentgen-ray unit with 8 animal cages at 2 meters from the source in position for exposure to the radial beam.

Animals which at autopsy were found to have a pre-existing chronic disease were discarded. The 115 swine that were found suitable for this study were allowed to die or were killed when

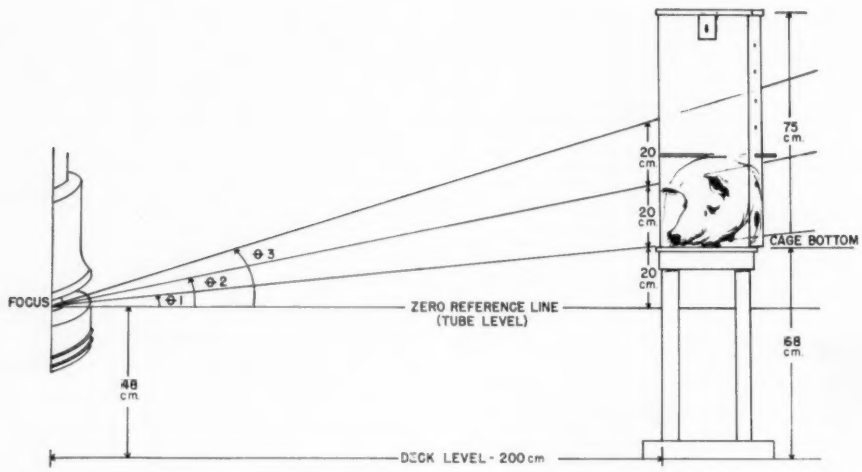


FIG. 2. Detail drawing to show portion of radial beam used for total body irradiation of a swine. Note that the sides of the animal touch the sides of the plywood cage and the animal is held in the prone position by means of adjustable through-and-through dowels.

$\theta_1 = \tan^{-1} 20/200 = 5.7°$ from horizontal or 95.7° from vertical — $\theta_2 = \tan^{-1} 40/200 = 11.3°$ from horizontal or 101.3° from vertical. $\theta_3 = \tan^{-1} 60/200 = 16.7°$ from horizontal or 106.7° from vertical.

moribund. All were autopsied as soon as possible after death.

## RESULTS

In establishing lethal dose curves for the unilateral and bilateral exposures, a few swine were subjected to the extreme high and low doses while the majority were concentrated in the mid-lethal dose range. Table 1 indicates the mortality percentages

TABLE I

MORTALITY IN SWINE EXPOSED TO UNILATERAL AND BILATERAL TOTAL BODY 2,000 kv. (peak) ROENTGEN RADIATION

| Dose Unilateral | No. of Swine Exposed | No. of Radiation Deaths | Per Cent Mortality | Deaths Day Post-irradiation | Dose Bilateral | No. of Swine Exposed | No. of Radiation Deaths | Per Cent Mortality | Deaths Day Post-irradiation |
|---|---|---|---|---|---|---|---|---|---|
| 200 r/1 | 4 | 0 | 0.0 | — | 200 r/2 | 4 | 0 | 0.0 | — |
| 250 r/1 | 0 | — | — | — | 250 r/2 | 3 | 0 | 0.0 | — |
| 300 r/1 | 0 | — | — | — | 300 r/2 | 8 | 5 | 63.0 | 11, 15, 16, 18, 21 |
| 350 r/1 | 4 | 0 | 0.0 | — | 350 r/2 | 8 | 7 | 87.5 | 13, 13, 14, 15, 16, 21, 24 |
| 400 r/1 | 8 | 0 | 0.0 | — | 400 r/2 | 6 | 3 | 50.0 | 13, 21, 22 |
| 450 r/1 | 7 | 2 | 28.5 | 10, 26 | 450 r/2 | 8 | 5 | 62.5 | 11, 11, 11, 12, 13 |
| 500 r/1 | 7 | 4 | 57.1 | 14, 15, 19, 25 | 500 r/2 | 9 | 8 | 88.8 | 11, 11, 11, 13, 13, 15, 17, 17 |
| 550 r/1 | 7 | 5 | 71.4 | 15, 16, 16, 19, 23 | 550 r/2 | 8 | 8 | 100.0 | 8, 12, 12, 12, 15, 17, 17, 17 |
| 600 r/1 | 8 | 8 | 100.0 | 10, 10, 13, 14, 14, 14, 14 | 600 r/2 | 4 | 4 | 100.0 | 11, 12, 12, 12 |
| 800 r/1 | 4 | 4 | 100.0 | 9, 9, 9, 11 | 800 r/2 | 4 | 4 | 100.0 | 9, 9, 9, 11 |

obtained with various doses of total body roentgen irradiation administered by the two methods. It will be noted that the first deaths among swine exposed unilaterally occurred after a total dose of 450 r, while only 300 r given bilaterally as a divided dose was sufficient to kill. All the animals receiving 600 r unilaterally or a total dose of 550 r bilaterally died.

With the lower doses, deaths occurred generally later and at wider spread time intervals than following the higher doses where deaths tended to occur earlier and tance to conform with the present 2,000 kv. (peak) experiments. It will be noted that curve *c* (Fig. 3) is distinct and separate from curve *a* (Fig. 3). The curves *b* and *c* in Figure 3 cannot be compared because sufficient data are not available to evaluate the small difference in biologic effect.

The estimated $LD_{50/30}$ is 350–400 r for the bilateral, divided dose, 2,000 kv. (peak) exposure, 500 r for the unilateral, single dose, 2,000 kv. (peak) exposure and 510 r for the bilateral, divided dose, 1,000 kv. (peak) exposure.

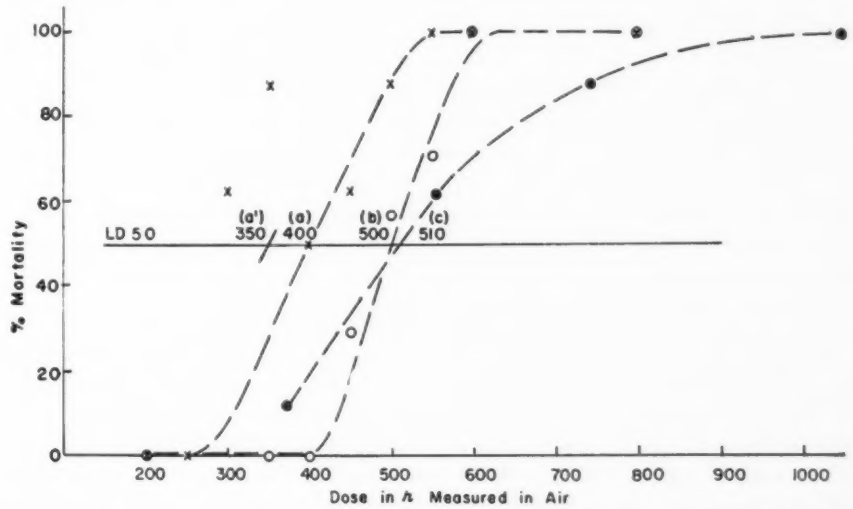


Fig. 3. Lethal dose curves in swine exposed to total body (*a*) and (*a'*) 2,000 kv. (peak) bilateral roentgen radiation, (*b*) 2,000 kv. (peak) unilateral roentgen radiation and (*c*) 1,000 kv. (peak) roentgen radiation, all at 2 meters target skin distance.

to be more closely grouped (Table 1). The variation in survival times is an expression of the variation in resistance to irradiation among the individual subjects.

When the results of the several experiments are plotted, sigmoid mortality curves are produced (Fig. 3). The bilateral 2,000 kv. (peak) exposure curve (*a*, Fig. 3) and the unilateral 2,000 kv. (peak) exposure curve (*b*, Fig. 3) are distinct and separate from each other.

It is interesting to compare *a* with *c* in Figure 3. In the latter case the exposure was bilateral, but the energy of the source was only 1,000 kv. (peak). The data for Figure 3*c* were taken from exposures at 1 meter target skin distance,[9] but were recalculated for 2 meters target skin dis-

The mortality percentages for the 300 r/2 and 350 r/2 doses appear to be completely out of line with the other bilateral exposure data (Table 1). The explanation may lie in the high incidence of pneumonia in these swine. All five deaths in the 300 r/2 group and 6 of the 7 deaths in the 350 r/2 group presented gross and/or histopathologic evidence at autopsy of pneumonia complicating radiation lesions. Conversely, none of the 3 deaths in the 400 r/2 group, only 2 of the 5 deaths in the 450 r/2 group and only 2 of the 8 deaths in the 500 r/2 group were complicated with pneumonia.

If all data are included, a free-hand fit mortality curve crosses the $LD_{50}$ line at 350 r (Fig. 3*a'*). The deduced $LD_{50/30}$ calculated by Behrens' method[1] is 350 r.

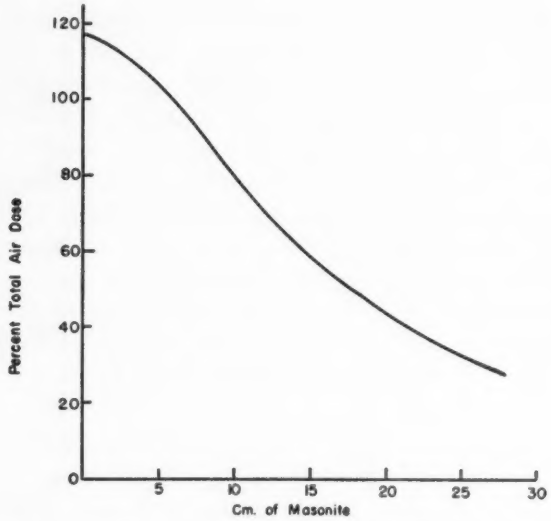


FIG. 4. Depth dose curve for 2,000 kv. (peak) roentgen radiation in a masonite phantom. Total dose given to one lateral aspect.

However, since the 300 r/2 and 350 r/2 points appear to be weighted due to the high incidence of pneumonia, it is our opinion that a more accurate $LD_{50/30}$ is obtained by disregarding these points. The free-hand fit curve after the stated omissions crosses the $LD_{50}$ line at 400 r as indicated in Figure 3, curve *a*.

With the few animals available, no significant difference in mortality in subjects exposed to left-side versus right-side unilateral irradiation was found. At 450 r/1, 5 of 7 left-sided exposures survived. There were no right-sided exposures. At 500 r/1, 3 of 4 left-sided exposures and 0 of 3 right-sided exposures survived. At 550 r/1, 1 of 4 left-sided and 1 of 3 right-sided exposures survived. At 600 r/1, there were no survivors of 4 left-sided and 4 right-sided exposures.

Gross and histopathologic examination of the swine which received lethal amounts of roentgen radiation revealed characteristic tissue changes. There was widespread cell destruction particularly evident in the relatively radiosensitive hematopoietic and lymphoid organs and the gastrointestinal mucosae. Widespread hemorrhage, not associated with manifest vascular damage, was the rule. Pneumonia was a common complicating disease beginning seven to ten days after irradiation. Terminal pulmonary edema was a frequent finding while terminal bacteremia (intestinal organisms) occurred in many of the swine.

In order to understand the differences in mortality produced by the 2,000 kv. (peak) exposures, depth dose values were plotted. Figure 4 shows the percentage total air dose distributed through 28 cm. of a masonite phantom when the dose is administered unilaterally. The entrance dose is 116 per cent while the exit dose is 26 per cent of the total air dose administered.

When the total air dose is divided so that one-half is administered to each lateral aspect of a masonite phantom, there are in effect two entrance and two exit doses. Curve *a* in Figure 5 is a mirror image of curve *b* in Figure 5 and each represents 50 per cent of the dose distribution through the phantom. The sum of curves *a* and *b* (Fig. 5) is curve *c* (Fig. 5) and represents the distribution of the total dose through the phantom. Thus the entrance dose of 58.5 per cent plus the exit dose of 13.5 per cent equals the total dose of 72 per cent to one lateral aspect (Fig. 5).

The areas under the curve in Figure 4 and curve *c* in Figure 5 are the same. This means that the total dose in both cases is the same. In spite of this fact, there is a marked difference in the distribution of

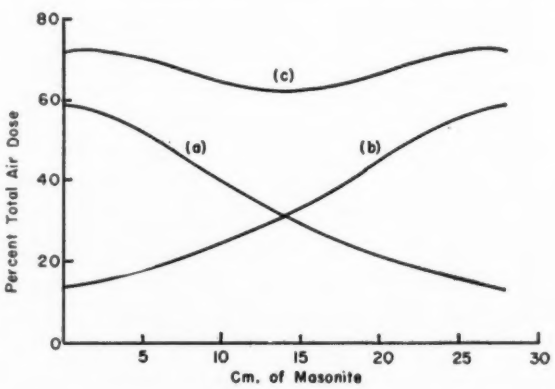


FIG. 5. Depth dose curves for 2,000 kv. (peak) roentgen radiation in a masonite phantom. (*a*) 50 per cent of total dose given to one lateral aspect. (*b*) 50 per cent of total dose given to opposite lateral aspect. (*c*) Total dose given 50 per cent to each lateral aspect (summation of curves *a* and *b*).

the dose throughout the phantom. Whereas, in the case of unilateral exposure, the entrance dose is 116 per cent and the exit dose is 26 per cent, in the case of bilateral exposure the combined entrance and exit dose to each lateral aspect is the same, 72 per cent. The dose at 14 cm. which corresponds to the median sagittal plane of the swine is the same in both cases.

Although the materials and methods used in the 1,000 kv. (peak) experiment[9] were different, a correction can be applied to give approximate values that will permit comparison with the 2,000 kv. (peak) data. Corrections for target skin distances from 1 to 2 meters and a phantom thickness from 25 to 28 cm. were calculated using the inverse square law. No correction was made for the difference in phantom material because of the short wavelength of the radiation employed.[5] The depth dose curves for 1,000 kv. (peak) radiation in Figure 6 were plotted in a manner similar to that employed in preparing curves for 2,000 kv. (peak) radiation in Figure 5. In curves *a* and *b* (fig. 6) the two entrance doses and the two exit doses are the same. The sum of curves *a* and *b* (Fig. 6) is curve *c* (Fig. 6) and represents the distribution of the total dose through the phantom. The entrance dose of 61.5 per cent plus the exit dose of 8.5 per cent equals the total dose of 70 per cent to each lateral aspect. The per cent total air dose at 14 cm., which corresponds with the median saggital plane of the swine, is 49.4.

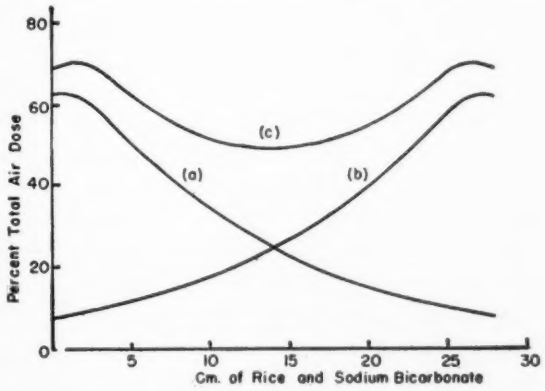


Fig. 6. Depth dose curves for 1,000 kv. (peak) roentgen radiation in a rice and sodium bicarbonate phantom. (*a*) 50 per cent total dose given to one lateral aspect. (*b*) 50 per cent total dose given to opposite lateral aspect. (*c*) Total dose given 50 per cent to each lateral aspect (summation of curves *a* and *b*).

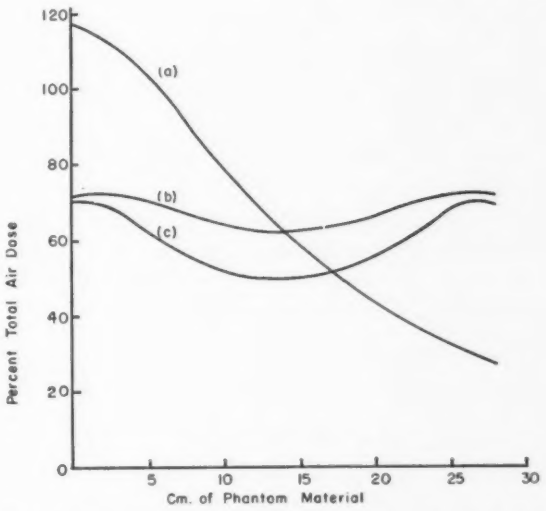


Fig. 7. Depth dose curves for 1,000 kv. (peak) and 2,000 kv. (peak) roentgen radiation. (*a*) Total dose of 2,000 kv. (peak) roentgen radiation given to one lateral aspect of a masonite phantom. (*b*) Total dose of 2,000 kv. (peak) roentgen radiation given 50 per cent to each lateral aspect of a masonite phantom. (*c*) Total dose of 1,000 kv. (peak) roentgen radiation given 50 per cent to each lateral aspect of a rice and sodium bicarbonate phantom.

In Figure 7 the curves represent the distribution of radiation in terms of per cent of total air dose. This permits a comparison of the dose at any given depth in the phantom for the three months of exposure.

The distribution of radiation in certain specific instances is presented in Table II. It is seen, for instance, that the bilateral divided administration provides much more even distribution of radiation than the unilateral single administration. The midline dose in 2,000 kv. (peak) unilateral and bilateral exposure is the same in both cases, 62.3 per cent of the total air dose. However, the phantom or animal receives very unequal doses on either side of the midline in the case of unilateral exposure. This lack of uniformity is reflected in the 2,000 kv. (peak) unilateral exposure $LD_{50/30}$ which is 100–150 r more than the $LD_{50/30}$ for 2,000 kv. (peak) bilateral exposure.

While the uniformity of the distribution

TABLE II

COMPARISON OF DOSE DISTRIBUTION AND 50 PER CENT MORTALITY USING THREE DIFFERENT IRRADIATION PROCEDURES

| Roentgen Irradiation Technique | Per Cent Total Air Dose Distributed throughout Phantom (averaged) | Per Cent Total Air Dose at Midline (14 cm.) | Per Cent Total Air Dose at One Lateral Aspect | Per Cent Total Air Dose at Opposite Lateral Aspect | $LD_{50/30}$ |
|---|---|---|---|---|---|
| 2,000 kv. (peak) unilateral administration | 67.5 | 62.3 | 116 | 26 | 500 r |
| 2,000 kv. (peak) divided administration | 67.5 | 62.3 | 72 | 72 | 350–400 r |
| 1,000 kv. (peak) divided administration | 59 | 49.4 | 70 | 70 | 510 r |

of the dose in the 1,000 kv. (peak) bilateral exposure is comparable with that in the 2,000 kv. (peak) bilateral exposure, there are important differences in the quantity of dose. The integrated and averaged percentage of total air dose through the 28 cm. phantom is 8.5 per cent less in the case of 1,000 kv. (peak) radiation. Peripherally, the total air dose percentages show little difference with the 1,000 and 2,000 kv. (peak) bilateral exposures, but in the midline the fall off with 1,000 kv. (peak) radiation is 12.9 per cent more than in the case of 2,000 kv. (peak) radiation.

## DISCUSSION

Since the mortality varies with the radiation technique employed, it is apparent that an important factor in considering the biologic effect of total body irradiation of large (thick) swine and human beings is the dose distribution throughout the body. With smaller laboratory animals in more common use, the entrance-exit dose ratio is close to 1 while with swine 28 cm. in thickness, the entrance-exit dose ratio is approximately 4.5. Where unilateral exposure is used, the mortality is less than that produced by bilateral exposure, even though a 2,000 kv. (peak) radiation source is employed for both methods and the air r exposure is the same.

A second factor responsible for differences in mortality in large animals exposed to equal air doses of roentgen radiation is the widely accepted one, variation in wavelength of the radiation. A comparison of the lethal dose curve obtained with bilateral exposure of swine to 2,000 kv. (peak) radiation (Fig. 3*a*) and that obtained with bilateral exposure of swine to 1,000 kv. (peak) (Fig. 3*c*) indicates a marked difference in response. The method of exposure remains the same in these two instances, but the lower energy source is unable to effect the uniformity of distribution of radiation within the large animal that is achieved with a higher energy source.

The difference between the $LD_{50/30}$ values of the 2,000 kv. (peak) and 1,000 kv. (peak) bilateral radiation is greater than would be expected from the phantom depth dose measurements. This discrepancy has two possible explanations. First, the unit density phantom does not truly represent the variable density animal body, and, secondly, although the central more radiosensitive organs receive less radiation than the more radioresistant, except rib marrow, peripheral organs in both cases, the difference is marked in the case of 1,000 kv. (peak) radiation.

Presumably, a very high energy source

at a suitable target skin distance can reduce the entrance-exit dose ratio in a thick subject to a figure close to 1. At present, with the experimental facilities readily available, the best way to achieve a uniform dose distribution in a thick object is to irradiate on each lateral aspect. The ideal is approached as the depth dose curve approaches a horizontal straight line with minimal or no central fall off. The lethal dose curves are at best only approximations. It is interesting that a straight line drawn through the highest dose at which there were no deaths and the lowest dose at which all animals died crosses the 50 per cent mortality line at 400 r in the bilateral 2,000 kv. (peak) radiation and at 500 r in the unilateral 2,000 kv. (peak) radiation. This is in conformity with the free-hand fit mortality curves. The margin of tolerance to total body roentgen irradiation is narrow, the range between zero and 100 per cent mortality in 2,000 kv. (peak) radiation being only 200 r. That most of the experimental points in the lethal range fall within narrow limits is testimony favoring the validity of the point values.

The experiments were not designed for and sufficient data are not available to discuss the effect of inherent body filtration on the spleen and/or liver, depending on whether the left or the right side is exposed in unilateral irradiation.

It is obvious that the irradiated animal is easy prey to secondary infections and that the infections may be the deciding factor in whether the animal lives or dies. Only in an artificial germ-free environment can a highly accurate, pure-system radiation lethal dose curve be established. The industrial or military use of atomic energy in a germ-free world will probably not prevail in the foreseeable future. Therefore, from a practical point of view, it is probably better to study radiation effects in an environment with a random germ population. The importance of judicious administration of appropriate antibiotics is evident.

## CONCLUSIONS

1. Two thousand kilovolts (peak) bilateral total body roentgen irradiation produces a greater mortality in large swine than 1,000 kv. (peak) bilateral total body roentgen irradiation.

2. Two thousand kilovolts (peak) bilateral total body roentgen irradiation produces a greater mortality in large swine than 2,000 kv. (peak) unilateral total body roentgen irradiation.

3. An important factor in determining the effectiveness of total body roentgen irradiation is the distribution of the dose in the body.

4. The thickness of the subject and the wavelength of the radiation govern the distribution of the dose.

The authors wish to thank Drs. H. T. Giltner and H. Seibold, of the USDA for reviewing some of these tissue sections, J. S. Otto, HMC, USN, J. T. Istock, HMC, USN, of NMRI, and the staff of the Radiology Section of the Naval Ordnance Laboratory, for their help and cooperation in conducting the experiments.

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## REFERENCES

1. Behrens, B. Zur Auswertung der Digitalisblätter im Froschversuch. *Arch. f. exper. Path. u. Pharmakol.*, 1929, *140*, 237–256.
2. Chambers, F. W., Jr., Morgan, J. E., and Istock, J. T. Output characteristics of commercial x-ray generator of 2000 KVP. Nav. Med. Res. Inst., Project NM 006 012.08.26, December 7, 1949.
3. Cronkite, E. P. Hemorrhagic syndrome of acute ionizing radiation illness produced in goats and swine by exposure to atomic bomb at Bikini, 1946. *Blood*, 1950, *5*, 32–45.
4. Cronkite, E. P. Hematology of Bikini animals. *Am. J. Path.*, 1947, *23*, 891–892.
5. Spiers, F. W. Materials for depth dose measurement. *Brit. J. Radiol.*, 1943, *16*, 90–97.
6. Tullis, J. L., and Warren, S. Gross autopsy observations in animals exposed at Bikini. *J.A.M.A.*, 1947, *134*, 1155–1158.
7. Tullis, J. L. Radioresistant cells in certain radiosensitive tissues of swine exposed to atomic bomb radiation. *Arch. Path.*, 1949, *48*, 171–177.
8. Tullis, J. L. Response of tissue to total body irradiation. *Am. J. Path.*, 1949, *25*, 829–851.
9. Tullis, J. L., Tessmer, C. F., Cronkite, E. P., and Chambers, F. W., Jr. Lethal dose of total-body x-ray irradiation in swine. *Radiology*, 1949, *52*, 396–400.

# DISAPPEARANCE RATE OF TAGGED SUBSTANCES FROM THE CIRCULATION OF ROENTGEN IRRADIATED ANIMALS*

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EXAGGERATED phagocytic activity and increased permeability of the capillary wall are among the basic changes noted in man and animals exposed to massive irradiation. Neither of these is well understood. The studies here described were originally undertaken to determine quantitatively the effect of ionizing radiation on the reticulo-endothelial system. In the initial experiments, all tests performed were complicated by what appeared to be an increased capillary permeability. It became desirable, therefore, to study systematically the rate of disappearance of various substances labeled with radioisotopes from the blood and to determine their presence in different organs by quantitative isotopic measurements. Radioautographs were made whenever feasible to obtain information on the exact localization of the injected isotope.

Of the labeled materials used in this study, homologous plasma is expected to be retained in the circulation of normal hosts, disappearing slowly as it is utilized. Heterologous plasma is presumed to be withheld at sites of antibody formation and slowly metabolized. Evans blue attaches itself to blood proteins,[2,15] but is removed from the circulation by a variety of tissues which retain it for several weeks.[23] Colloidal gold is known to be withheld by reticulo-endothelial cells.[19] Homologous red cells are expected to circulate as do the erythrocytes of the hosts unless they are of a different type, or have been injured. Heterologous erythrocytes are engulfed by macrophages in which they are rapidly broken up. The rate of disappearance and the fate of such substances was studied to investigate differences in capillary permeability and macrophage function between normal and roentgen irradiated animals.

## METHODS

*Labeled Plasma.* The plasma was iodinated with $I^{131}$ by the method of Fine and Seligman[6] with one modification.[23]

*Labeled Red Cells.* The erythrocytes were tagged with $P^{32}O_4$ by the procedure first developed by Hevesy and Zerahn[11] and later modified by Nieset *et al.*[14]

*Labeled Colloidal Gold.* Five milligrams of pure gold metal were irradiated in the Oak Ridge reactor for sixty-two hours, thus assuring a relatively high percentage of the radioisotope $Au^{198}$. The gold was dissolved in aqua regia and the excess acid removed by moderate heating under vacuum.[19] The "$AuCl_3$" residue was taken up in distilled water, giving a final concentration of 0.05 mg/ml. The pH was adjusted to 3.5 to 3.7 with NaOH and the gold salt was converted to colloidal gold, employing trisodium citrate as the reducing agent.[12] The pH rose to 6.9 to 7.0 after the dispersion. The solution was centrifuged at about 1,500 g to remove large particles. In some experiments the colloid was mixed with an equal volume of plasma before injection.

Electron microscope pictures of this type of sol showed the particles to be spherical and fairly homogeneous in size with a diameter of 5 to 10 $\mu$. This homogeneity was confirmed by moderately sharp boundaries between phases in the analytical ultracentrifuge at 9,000 to 10,000 r.p.m. Attempts to produce a smaller colloid resulted in incomplete dispersal with significant amounts of undispersed gold present as shown by the o-tolidine tests.[21] Redox potential measurements and absence of color of the solutions indicated minimal amounts of gold chloride and suggested that almost all undispersed gold was complexed with citrate ions. Larger sols may be easily prepared by lowering the initial pH.

*Radioactivity Determinations.* All $P^{32}$ samples were counted with a Tracerlab autoscaler equipped with automatic sample changer and printing timer. The

* Work performed in the Biology Division of Oak Ridge National Laboratory under Contract No. W-7405-eng-26 for the Atomic Energy Commission.

blood was pipetted directly into counting capsules, diluted with distilled water, and evaporated to dryness under a heat lamp. The same volume of blood was added to all standards in order to have a similar solid content and hence a similar self-absorption, although this was small under these experimental conditions. Tissues were wet-ashed with concentrated $HNO_3$ and 30 per cent $H_2O_2$, and aliquots pipetted for counting. Precautions were taken to avoid any significant self-absorption error.

Biological substances containing $I^{131}$ and $Au^{198}$ were assayed for radioactivity either in a gamma-ray ionization chamber,[20] into which were inserted suitable lusteroid tubes containing the tissue or blood, or in a manner similar to that described above for $P^{32}$.

*Evans Blue Determinations.* The optical density of Evans blue solutions was determined in a Beckman spectrophotometer, using a Lowry cell.[13] Corrections were made for any possible hemolysis as suggested by Gibson and Evans.[8]

*Experimental Animals.* Some of the rabbits used were inbred Dutch hybrid animals weighing about 2,000 grams, approximately three to six months old, and were raised in this laboratory. Others were purchased albino rabbits, weighing approximately 3,500 grams. The latter animals were used in preliminary experiments while the more uniformly reacting, inbred animals served in final tests.

All mice used in the experiment were young adults either of the Ak or Rf stock raised in this laboratory. They were carefully matched in each experiment for uniformity of weight, age, and sex. The intravenous injections in mice were made under light nembutal anesthesia. All animals were autopsied at death.

*Factors of Irradiation.* Rabbits received 1,000 r and mice 575 r of roentgen rays, an approximate $LD_{50}$ dose. Two machines were used in all the experiments and the factors of irradiation were as follows:

Machine 1—General Electric "Maximar," 250 kv. (peak), 15 ma., half-value layer 0.4 mm. Cu; inherent filtration 3 mm. Al. The output and target skin distance for mice were 59 r/min. and 92.3 cm., respectively, and for rabbits 90 r/min. and 71.0 cm.

Machine 2—General Electric "Maxitron," 250 kv. (peak), 30 ma., half-value layer 0.5 mm. Cu; inherent filtration <1.0 mm. Al, with 3 mm. Al added. The output and target skin distance for mice were 66 r/min. and 93.7 cm., respectively. For rabbits the dose rates were 82 r/min. (skin) and 59 r/min. (internal) at a target-skin distance of 93.7 cm.

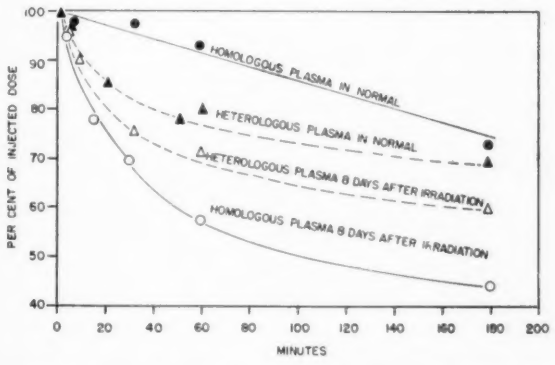
PER CENT OF INJECTED DOSE
MINUTES
HOMOLOGOUS PLASMA IN NORMAL
HETEROLOGOUS PLASMA IN NORMAL
HETEROLOGOUS PLASMA 8 DAYS AFTER IRRADIATION
HOMOLOGOUS PLASMA 8 DAYS AFTER IRRADIATION

Fig. 1. Disappearance of $I^{131}$-labeled plasma after intravenous injection from the blood of a normal rabbit and of a rabbit eight days after exposure to 1,000 r.

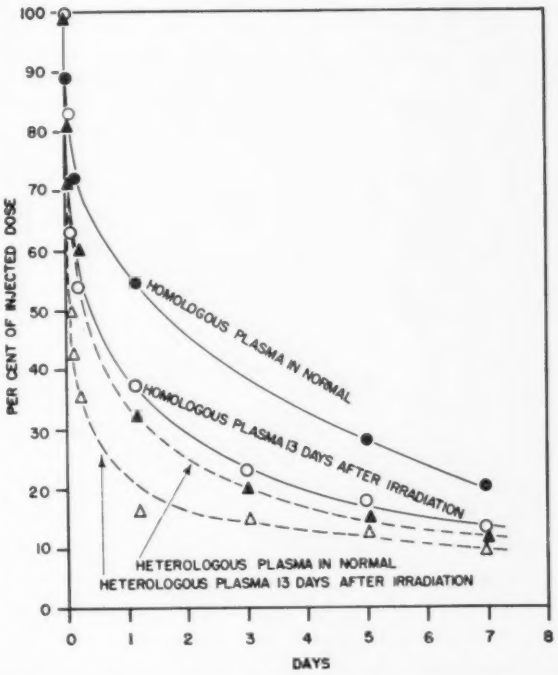
PER CENT OF INJECTED DOSE
DAYS
HOMOLOGOUS PLASMA IN NORMAL
HOMOLOGOUS PLASMA 13 DAYS AFTER IRRADIATION
HETEROLOGOUS PLASMA IN NORMAL
HETEROLOGOUS PLASMA 13 DAYS AFTER IRRADIATION

Fig. 2. Disappearance of $I^{131}$-labeled plasma after intravenous injection from the plasma of a normal rabbit and of a rabbit thirteen days after exposure to 1,000 r.

## RESULTS

I. *Homologous and Heterologous Plasma.* In a series of experiments, $I^{131}$-labeled homologous or heterologous (dog) plasma was injected intravenously into normal and irradiated rabbits; the latter received 1,000 r one to thirteen days before injection. Blood samples were withdrawn at intervals, usually up to two hours but sometimes up to seven days after the injection, and the per cent of injected dose found in the plasma was plotted against time. Figures 1 and 2 show the results of representative experiments eight and thirteen days after irradiation, respectively. The curves are similar,

TABLE I

PER CENT DISAPPEARANCE OF HOMOLOGOUS AND HETEROLOGOUS (DOG) PLASMA LABELED WITH $I^{131}$ FROM THE BLOOD OF IRRADIATED AND NORMAL RABBITS 30 MINUTES AFTER INTRAVENOUS INJECTION

| Days After Irradiation | Homologous | | | Heterologous | | |
|---|---|---|---|---|---|---|
| | Normal | Roentgen Irradiated | Roentgen Irradiated / Normal | Normal | Roentgen Irradiated | Roentgen Irradiated / Normal |
| 1 | ♀ 15.5 | ♀ 15.6 | 1.01 | ♀ 13.0 | ♂ 12.1 | 0.93 |
| 2 | ♀ 21.8 | ♀ 19.0 | 0.87 | ♀ 18.5 | ♀ 19.1, 22.5 | 1.03, 1.22 |
| 3 | ♂ 5.0 | ♂ 21.5 | 4.30 | ♀ 25.5 | ♀ 30.0 | 1.18 |
| 4 | ♀ 11.1 | ♀ 26.4 | 2.38 | — | — | — |
| 5 | — | — | — | ♀ 13.5 | ♂ 20.0 | 1.48 |
| 6 | ♀ 15.6 | ♀ 23.0 | 1.47 | ♀ 16.6 | ♀ 22.8 | 1.37 |
| 7 | — | — | — | ♂ 17.5 | ♂ 30.0 | 1.71 |
| 8 | ♀ 4.5 | ♀ 30.6 | 6.80 | ♀ 17.5 | ♀ 24.1 | 1.38 |
| 9 | ♀ 21.3 | ♀ 10.0 | 0.89 | ♀ 14.2 | ♀ 23.6 | 1.66 |
| 11 | ♂ 5.6 | ♂ 10.3 | 1.84 | — | — | — |
| 13 | ♂ 5.6 | ♂ 20.7 | 3.70 | ♂ 15.0 | ♂ 43.7 | 2.91 |
| 21 | ♀ 9.1 | ♀ 16.6 | 1.83 | — | — | — |

consisting of an initial rapid disappearance for thirty minutes followed by a much slower rate for several days (Fig. 2). The thirty minute value was arbitrarily chosen as an index suitable for expressing the difference between normal and roentgen irradiated animals.

The results of 10 experiments are summarized in Table 1.

After the second day, the disappearance rate of plasma was faster in roentgen irradiated animals than in the controls, with one exception (the animal receiving homologous plasma 9 days after irradiation). The ratios of disappearance rates (irradiated over normal) were much greater with homologous than with heterologous plasma (Table 1).

II. *Evans Blue.* As the Evans blue dye combines with the plasma proteins,[15] the increase in disappearance rate from the blood of irradiated animals as compared to that of normal animals may be related in part to the degree of capillary permeability.

Blood samples were obtained from rabbits at six and thirty minutes after intravenous injection of this dye. Assuming that the six minute sample represented maximum concentration of the dye in the blood, the difference between the six minute and the thirty minute samples, expressed in per cent of the injected dose, was taken as

TABLE II

PER CENT DISAPPEARANCE OF EVANS BLUE (T-1824) FROM THE BLOOD OF NORMAL AND IRRADIATED RABBITS 30 MINUTES AFTER INTRAVENOUS INJECTION

| Days After Irradiation | Sex | Normal | Roentgen Irradiated | Roentgen Irradiated / Normal |
|---|---|---|---|---|
| 1 | ♀ | 16 | 8 | 0.5 |
| 1 | ♀ | 18 | 20 | 1.1 |
| 2 | ♀ | 16 | 20 | 1.3 |
| 2 | ♂ | 17 | 15 | 0.9 |
| 2 | ♂ | 14 | 17 | 1.2 |
| 4 | ♂ | 13 | 13 | 1.0 |
| 4 | ♂ | 15 | 19 | 1.3 |
| 5 | ♂ | 15 | 19 | 1.3 |
| 7 | ♂ | 12 | 19 | 1.6 |
| 8 | ♀ | 15 | 18 | 1.2 |
| 14 | —* | 7 | 18 | 2.6 |
| 14 | —* | 15 | 15 | 1.0 |
| 17 | ♀ | 16 | 20 | 1.3 |

* In these experiments the controls were females (♀) and the roentgen irradiated animals males (♂).

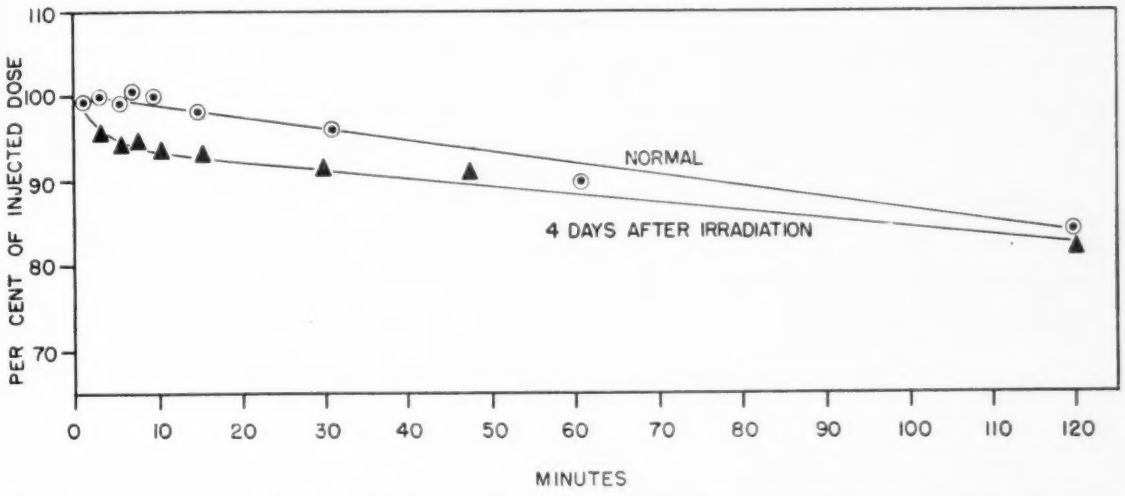


Fig. 3. Disappearance of "autoerythrocytes" labeled with $P^{32}$ from the blood of rabbits after intravenous injection.

the thirty minute disappearance value. This value was employed for comparing the disappearance rates of this dye in normal and irradiated animals.

Table II summarizes the per cent disappearance of Evans blue from the blood of normal and irradiated animals thirty minutes after intravenous injection, during the period of one to seventeen days after irradiation. After the second day the ratio of disappearance (irradiated over normal) was either unity (2 rabbits) or above unity (6 rabbits).

III. *Homologous Erythrocytes.* In order to exclude type differences which might exist among rabbits, blood withdrawn and tagged was reintroduced into the same animal. Approximately 3 ml. was removed from each animal, 1 ml. of which was used for determination of activity of the labeled blood and 1 ml. reinjected into the rabbit for determination of disappearance curves. There was no evidence of hemolysis during the tagging procedure.

Disappearance curves of $P^{32}$-labeled erythrocytes from normal and roentgen irradiated rabbits (4 days after irradiation) are shown in Figure 3. In the normal rabbit, the labeled erythrocytes disappear from the blood at a nearly constant rate; in the irradiated rabbit there is an initial rapid disappearance for twenty minutes after which the rate is similar to that of the normal. Therefore, the twenty minute values have been selected for comparison and are summarized in Table III for one to fifteen days after irradiation. In all cases the ratio of irradiated to normal is greater than unity with a range of 1.3 to 3.9. There appears to be little, if any, relationship between time of irradiation and this ratio, although two of the smallest values (1.9 and 1.3) occur soon after irradiation.

IV. *Heterologous Erythrocytes.* Erythrocytes are a classical material for assay of phagocytic function, since they can be readily visualized and their uptake by reticulo-endothelial cells is a normal proc-

Table III

PER CENT DISAPPEARANCE OF "AUTOERYTHROCYTES" LABELED WITH $P^{32}$ FROM THE BLOOD OF NORMAL AND IRRADIATED RABBITS 20 MINUTES AFTER INTRAVENOUS INJECTION

| Days After Irradiation | Normal | Roentgen Irradiated | Roentgen Irradiated / Normal |
|---|---|---|---|
| 1 | 4.0 | 7.5 | 1.9 |
| 2 | 4.0 | 11.0 | 2.8 |
| 4 | 2.5 | 8.0 | 3.2 |
| 5 | 2.5 | 3.3 | 1.3 |
| 6 | 2.0 | 6.7 | 3.9 |
| 8 | 2.5 | 6.5 | 2.6 |
| 10 | 3.5 | 8.4 | 2.4 |
| 15 | 2.0 | 6.7 | 3.9 |

TABLE IV

PER CENT OF $P^{32}$ LABELED HETEROLOGOUS (RABBIT) ERYTHROCYTES REMAINING IN THE BLOOD AND ORGANS OF NORMAL AND IRRADIATED MICE AT VARIOUS TIMES AFTER INTRAVENOUS INJECTION

| Organ | Control | | | | 1 Day After Roentgen Irradiation | | | | 4 Days After Roentgen Irradiation | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 5 min. | 30 min. | 120 min. | 19 hr. | 5 min. | 30 min. | 120 min. | 19 hr. | 5 min. | 30 min. | 120 min. | 19 hr. |
| *Experiment A* | | | | | | | | | | | | |
| Blood | 20.3 | 4.0 | 1.6 | 1.4 | 31.5 | 5.5 | 1.6 | 1.4 | 13.4 | 6.3 | 1.4 | 1.4 |
| Liver | 46.2 | 70.7 | 37.4 | 11.4 | 28.0 | 70.2 | 12.7 | 7.5 | 57.7 | 67.5 | 42.7 | 11.2 |
| | *27.2* | *40.6* | *24.0* | *5.6* | *19.9* | *42.5* | *8.6* | *4.9* | *33.2* | *65.5* | *31.2* | *8.1* |
| Spleen | 1.9 | 5.4 | 2.2 | 1.2 | 1.4 | 1.4 | 2.5 | 0.7 | 0.5 | 0.7 | 1.0 | 0.3 |
| | *19.6* | *23.4* | *14.6* | *6.3* | *13.3* | *19.3* | *27.3* | *8.3* | *10.4* | *16.6* | *21.3* | *9.4* |
| Kidneys | 1.4 | 1.9 | 4.6 | 1.6 | 2.3 | 2.2 | 3.9 | 1.7 | 1.5 | 2.0 | 3.4 | 1.7 |
| | *2.7* | *3.4* | *7.7* | *2.4* | *5.7* | *4.0* | *8.1* | *3.5* | *2.9* | *5.0* | *8.2* | *5.6* |
| | Control | | | | 7 Days After Roentgen Irradiation | | | | 15 Days After Roentgen Irradiation | | | |
| *Experiment B* | | | | | | | | | | | | |
| Blood | 9.3 | 4.0 | 2.0 | 1.6 | 29.0 | 2.3 | 2.0 | 1.4 | 5.1 | 6.5 | 1.9 | 1.0 |
| Liver | 76.1 | 65.1 | 38.0 | 11.0 | 50.0 | 79.0 | 37.2 | 12.4 | 91.2 | 77.5 | 42.5 | 16.8 |
| | *34.0* | *36.6* | *22.8* | *5.5* | *35.2* | *68.8* | *27.1* | *7.3* | *57.1* | *46.8* | *25.8* | *8.4* |
| Spleen | 2.0 | 5.0 | 2.1 | 1.0 | 0.8 | 0.3 | 1.0 | 0.2 | 0.5 | 2.3 | 1.9 | 1.6 |
| | *12.2* | *37.4* | *28.0* | *5.7* | *20.3* | *10.4* | *25.0* | *5.7* | *5.2* | *19.1* | *13.4* | *8.5* |
| Kidneys | 1.1 | 2.7 | 4.1 | 1.7 | 1.6 | 1.9 | 3.2 | 1.6 | 0.7 | 1.2 | 3.7 | 1.9 |
| | *1.7* | *5.0* | *7.6* | *3.1* | *4.2* | *5.9* | *8.5* | *4.6* | *1.6* | *2.3* | *6.4* | *3.3* |
| Lungs | 0.9 | 3.8 | 0.5 | 0.4 | 8.6 | 1.7 | 0.7 | 0.4 | 2.7 | 1.7 | 0.7 | 0.4 |
| | *4.6* | *22.4* | *3.2* | *2.5* | *62.2* | *12.9* | *4.8* | *2.9* | *18.4* | *10.7* | *3.8* | *2.4* |
| Urine | — | — | — | 12.7 | — | — | — | 12.6 | — | — | — | 7.5 |

The figures indicate the per cent of injected activity (dose). Those in italics indicate per cent of injected activity per gram of tissue.

ess. It was thought that the study of the fate of heterologous erythrocytes in normal and irradiated animals might yield information on reticulo-endothelial function.

In the experiments recorded in Table IV, the radioactivity of the blood of normal and irradiated mice was assayed at five, thirty, 120 minutes and nineteen hours after intravenous injection of labeled rabbit erythrocytes. It was found that the rabbit erythrocytes were removed very rapidly from the blood of both normal and irradiated mice, the per cent remaining in five minutes ranging from 5.1 to 31.5 (Table IV). This wide range is probably caused by slight differences along a very steep disappearance curve. The behavior of the heterologous cells in the blood stream resembles that of large colloidal particles and other forcign bodies. Thirty minutes after injection, 93 to 98 per cent of the radioactivity has been removed from the circulation; but thereafter the rate of removal is extremely slow, with from 1 to 2 per cent remaining in the blood in the interval of 120 minutes to nineteen hours.

This residual activity may be either $P^{32}$ liberated from the phagocytosed erythrocytes into the plasma or $P^{32}$ exchanged between cells and plasma. The latter process was found to proceed at a rate of approximately 5 per cent/hour for homologous cells.[16]

Approximately 70 to 90 per cent of the radioactivity was found in the liver and spleen within the first thirty minutes after injection, but in two hours there was a drop to a much lower level. This decrease continued slowly, so that in twenty hours these two organs contained about 10 per cent of the injected dose. The sharp rise and fall of $P^{32}$ in the liver and spleen suggests that the heterologous cells are first rapidly phagocytosed and soon thereafter are broken down, resulting in a release of $P^{32}$ into the surrounding tissues. Radioautographs of these tissues showed an over-all blackening from the diffuse spreading of the $P^{32}$ throughout the area of phagocytosis.

It is noteworthy that the spleen of the roentgen irradiated animal contained less activity (injected cells) than the spleen of the normal animal. This organ shrinks to about one-third of its original weight over a period of about eight days after irradiation. However, the concentration expressed as per cent of injected dose per gram of tissue was similar in both controls and irradiated mice. Thus, although the spleen had undergone marked atrophy, the macrophage tissue had a nearly normal phagocytic capacity.

The $P^{32}$ released from lysed erythrocytes probably re-enters the blood stream very slowly as inorganic $P^{32}$ and is metabolized and/or excreted. The $P^{32}$ activity of the kidneys increased with time. The 120 minute value was maximum in all cases and the nineteen hour value was about 50 per cent of this maximum. The urine collected for nineteen hours in Experiment B contained 7.5 to 12.7 per cent of the injected $P^{32}$ (Table IV.)

The lungs were assayed in the second experiment (Table IV). Those of the irradiated animals had the maximum $P^{32}$ activity in five minutes after injection (2.7 to 8.6 per cent of the injected dose), and the controls in thirty minutes (3.8 per cent of the injected dose). In nineteen hours the $P^{32}$ activity of the lungs of all animals dropped to about 0.4 per cent.

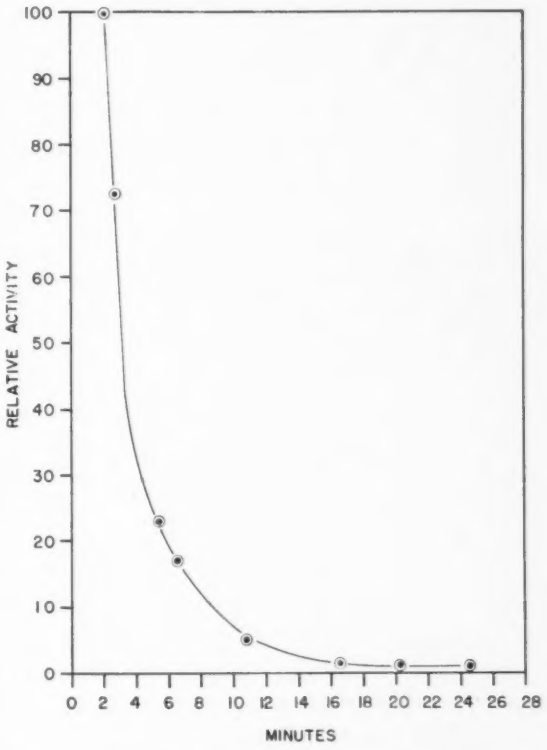


Fig. 4. Rate of disappearance of colloidal $Au^{198}$ from blood of a rabbit after intravenous injection.

V. *Colloidal Gold.* Colloidal gold labeled with $Au^{198}$ was injected into normal and roentgen irradiated rabbits, one, three, five, and eight days after irradiation. Three sols each similarly prepared gave disappearance curves with a half-value time of 1.5 to 2.5 minutes (Fig. 4), as found earlier.[3] Table V shows the per cent of injected $Au^{198}$ retained in the blood five and twenty minutes after injection, assuming a plasma volume as reported elsewhere.[22] These results indicate that the ratio of values in normal to roentgen irradiated animals ranges from 1.1 to 2.0 at five minutes and from 3.2 to 8.7 at twenty minutes.

Colloid A preparations disappeared from

TABLE V

PER CENT COLLOIDAL $Au^{198}$ RETAINED IN THE BLOOD OF NORMAL AND IRRADIATED FEMALE RABBITS AFTER INTRAVENOUS INJECTION

| Colloid | Days After Irradiation | Time after Injection: 5 min. Normal | 5 min. Roentgen Irradiated | 5 min. Normal / Roentgen Irradiated | 20 min. Normal | 20 min. Roentgen Irradiated | 20 min. Normal / Roentgen Irradiated |
|---|---|---|---|---|---|---|---|
| A | 1 | 38.6 | 19.7 | 2.0 | 21.2 | 6.6 | 3.2 |
| A | 3 | 47.5 | 23.4 | 2.0 | 22.5 | 2.6 | 8.7 |
| B | 5 | 21.0 | 14.4 | 1.5 | — | — | — |
| B | 5 | 22.0 | 19.1 | 1.2 | — | — | — |
| B | 5 | 22.0 | 20.2 | 1.1 | — | — | — |
| C | 8 | 21.5 | 13.4 | 1.6 | — | — | — |
| C | 8 | 23.4 | 14.5 | 1.6 | 2.8 | 0.6 | 4.7 |

the blood about twice as slowly as B and C, although the method of preparation and the physical characteristics of each were similar. Gofman[9] recently has presented evidence of a relationship between the size of colloidal particle and the rate of disappearance, smaller particles being removed more slowly. A more exacting study of the physical nature of these colloids and of the mechanism of phagocytosis is necessary for a better understanding of the relationship between disappearance rate and colloidal size. After intravenous injection colloidal gold is rapidly phagocytosed by the liver and spleen of normal animals, so that a large fraction is found in these organs within a few minutes.

Labeled colloid was injected into the tail vein of mice irradiated eleven days previously, and into controls. The animals were sacrificed ten minutes after injection and their livers and spleens assayed for colloidal $Au^{198}$. Table VI lists the weight of these organs, the per cent of the injected dose, and the per cent activity per gram of tissue. The livers of the irradiated mice weighed about 70 per cent of those of the controls and the spleens about 30 per cent. However, the absolute amount of $Au^{198}$ activity was approximately the same for both normal and irradiated mice, while the activity per gram of tissue rose sharply in the irradiated mice, indicating that the macrophage function was not diminished

TABLE VI

PER CENT COLLOIDAL $Au^{198}$ RETAINED IN THE LIVER AND SPLEEN OF MICE 10 MIN. AFTER INTRAVENOUS INJECTION

| Animal | Liver Wt. gm. | Liver Injected dose | Liver Activity per gm. of tissue | Spleen Wt. gm. | Spleen Injected dose | Spleen Activity per gm. of tissue |
|---|---|---|---|---|---|---|
| | | per cent | per cent | | per cent | per cent |
| Control | 1.62 | 92.3 | 57.0 | 0.124 | 1.9 | 15.4 |
| Control | 1.65 | 95.7 | 57.7 | 0.167 | 3.5 | 21.0 |
| 11 days after 620 r | 1.19 | 94.6 | 79.5 | 0.053 | 3.7 | 69.8 |
| 11 days after 620 r | 1.03 | 97.1 | 94.4 | 0.053 | 2.5 | 41.7 |

TABLE VII

PER CENT OF INJECTED COLLOIDAL $Au^{198}$ FOUND IN THE TISSUES OF MICE AT VARIOUS TIMES AFTER INTRAVENOUS INJECTION

| Tissue | Time after Injection | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 20 min. | 45 min. | 90 min. | 3 hr. | 20 hr. | 43 hr. | 73½ hr. | 96 hr. | 120 hr. |
| Liver | 40.8 | 70.6 | 76.6 | 84.7 | 83.2 | 83.2 | 83.7 | 85.1 | 82.3 |
| Spleen | 1.0 | 2.1 | 2.7 | 3.0 | 2.3 | 2.8 | 3.0 | 3.7 | 2.0 |
| Kidneys | 2.8 | 0.9 | 0.8 | 0.4 | 0.4 | 0.4 | 0.3 | 0.3 | 0.3 |
| Lungs | 1.7 | 1.0 | 0.3 | 0.2 | 0.1 | 0 | 0 | 0 | 0 |
| Intestinal tract | 10.3 | 5.6 | 6.3 | 2.0 | 1.6 | 4.6 | 2.0 | 2.0 | 2.0 |
| Tail | 3.3 | 2.7 | 3.9 | 1.6 | 2.1 | 1.5 | 2.2 | 1.8 | 2.6 |
| One Femur (bone marrow) | — | 0.5 | 0.3 | 0.3 | 0.4 | 0.2 | 0.3 | 0.2 | 0.4 |
| Carcass (remaining) | 36.7 | 21.4 | 11.2 | 9.3 | 10.6 | 11.0 | 10.6 | 9.3 | 10.0 |
| TOTAL | 96.6 | 104.8 | 102.1 | 101.5 | 100.7 | 103.7 | 102.1 | 102.4 | 99.6 |

One mouse was used at each time interval.

by irradiation. A similar conclusion was recently arrived at by Barrow *et al.*[3] in rabbits.

Most antigenic substances circulate in the blood stream for some time, and it is difficult to determine their fate. Since colloidal gold is removed rapidly and almost completely by the macrophage system, it is of interest to note the results of experiments in which a material balance of injected $Au^{198}$ colloid was made. Table VII shows the distribution of $Au^{198}$ colloid after twenty minutes when the activity in the heart blood is already negligible. Activity is maximum at twenty minutes and is gradually diminishing thereafter in the following organs: intestine, kidneys, lungs, and "remaining carcass." Activity is lowest at twenty minutes in the liver and spleen, reaching near maximum at three hours (84.7 per cent of total activity in liver and 3 per cent in spleen).

In mice killed within a few minutes after injection, a few black granules were noted along the endothelial lining of capillaries, but almost all gold was concentrated within reticulo-endothelial cells. Although the gold particles injected were submicroscopic, microscopic black granules of varying sizes appeared in reticulo-endothelial cells in large numbers within a few minutes. In the corresponding locations radioautographs showed the characteristic $\beta$ tracks. It is to be remembered that a large amount of the gold injected is carrier and not radioactive. The change of microscopically invisible to visible gold particles has also been noted by Goldie and Hahn.[10]

## DISCUSSION

*Disappearance Rates in Relation to Time after Irradiation.* The following is a summary of the observed ratios of disappearance rates in roentgen irradiated to normal rabbits:

| Days after Irradiation | Homologous Plasma | Heterologous Plasma | Autologous Erythrocytes | Evans Blue |
|---|---|---|---|---|
| 1 | 1.0 | 0.9 | 1.9 | 0.8 |
| 2–5 | 2.3 | 1.2 | 2.4 | 1.2 |
| 6–9 | 3.1 | 1.5 | 3.2 | 1.4 |
| 10–13 | 2.8 | 2.9 | 2.4 | — |
| 14–17 | — | — | 3.9 | 1.3 |
| 21 | 1.8 | — | — | — |

This tabulation shows that: (a) one day after irradiation the permeability change was less than on all subsequent days, and (b) there was a maximum alteration in six to thirteen days. This is in accord with known observations that the maximum hemorrhagic tendency in rabbits exposed

to an $LD_{50}$ of roentgen rays occurs in eleven to twelve days. Therefore, one might anticipate that the disappearance rates would be greatest in this interval. A correlation between hemorrhagic tendency and disappearance rates would be desirable.

*Interpretation of Increased Disappearance Rates in Roentgen Irradiated Animals.* The results of experiments with tagged plasma and Evans blue are best explained by assuming that the heightened disappearance rate of these substances in roentgen irradiated animals is due to an increase in capillary permeability. The most convincing data in favor of this view are those obtained with tagged erythrocytes. Both homologous and heterologous red cells were found to disappear more rapidly from the blood of irradiated animals than from the blood of normal controls. It is possible that irradiation *in vivo* has made the cells more vulnerable but the sum total of observations suggest that this is not the case; erythrocytes are not injured by the doses of roentgen rays used.[7]

The possibility of a heightened permeability in roentgen irradiated animals was investigated by sampling thoracic duct lymph.[4] Normal lymph contains only a small number of red blood cells—less than 10 per cent of the lymphocytes present. The lymph of massively irradiated animals, on the contrary, is often grossly bloody at six to thirteen days after exposure. This indicates a marked capillary damage, resulting in an increased disappearance rate of introduced foreign matter from the blood of roentgen irradiated animals. Since the lymph is ultimately drained back into the venous system, an equilibrium may be expected to be reached in both normal and irradiated animals.

The hemorrhagic manifestations in roentgen irradiated animals are well known.[1] They vary with the species, the dose of roentgen rays, and the time after irradiation. They occur in rabbits, but are more marked in dogs, guinea pigs and man. An anatomic manifestation of the hemorrhagic tendency is the presence of red blood cells in the lymph sinuses[5,7] where extravasated cells are phagocytosed and metabolized by macrophages. Erythrophagocytosis in lymph sinuses is marked in roentgen irradiated mice and occurs even in the absence of gross manifestations of a hemorrhagic tendency. This familiar pathological finding might be taken as evidence of escape of erythrocytes into tissue space in irradiated animals due to an increased capillary permeability.

The initial rapid drop in the activity of the blood of roentgen irradiated animals following the injection of labeled homologous cells would be difficult to account for in the absence of observations made on the lymph of irradiated animals. The possibility of a regularly occurring sudden initial drop in the circulating red cells immediately after injection is indeed difficult to comprehend. A partial loss of the labeling agent from the injected cells, occurring immediately after injection, is scarcely probable. The general shape of the curve suggests that the labeled cells are disappearing from the circulation by a process of steady exchange with some cellular pool which is not in direct and easy communication with the majority of the circulating blood. The lymph system could be this pool. It is conceivable that "sludging" occurs in the capillaries of irradiated animals, but the finding of many erythrocytes in the circulating lymph suggests that in the irradiated animals there is a cellular pool outside the main vascular tree and that part of of this pool at least is the lymph.

The determination of exchange rates by the isotope method in an equilibrium system of two compartments is discussed elsewhere.[18] Determination by isotopes of the transport of substances in a physiological system is of limited value when only one compartment is available for assessment. Nevertheless, assuming that an effective single extravascular compartment exists which is exchanging erythrocytes with the circulation, the curve in Figure 3 can be interpreted by supposing an exchange rate of approximately 70 per cent of the intra-

vascular cells per hour and an extravascular compartment containing about 5 per cent of the total cell mass. Further work is needed to assay the magnitude of this rate of loss in relation to dose of roentgen rays and the time after irradiation. It is possible that both processes, stasis with sludging, and passage of erythrocytes into a second compartment, occur concurrently. If the former occurs, the results of blood volume determinations require a re-evaluation as obstruction of capillaries by sludged cells would interfere with the free mixing of introduced materials. On the other hand, sludging itself would cause anoxia with resulting increased capillary permeability.

*Comparison of Disappearance Rates of Homologous and Heterologous Plasma.* The experiments with iodinated plasma show that both homologous and heterologous plasma disappear from the blood of irradiated animals more rapidly than from that of normal controls. The greater disappearance of heterologous as compared to homologous plasma is anticipated, but homologous plasma is not expected to leave the circulation as fast as some of the values found would indicate. Electrophoretic analyses showed no detectable changes in the plasma resulting from the iodination procedure. If type differences exist among rabbits when plasma is injected some variations in disappearance rate might occur because of a possible selective withdrawal of immune globulins. Also, the disappearance rate of heterologous plasma would vary according to quantitative differences in protein fractions—notably in immune globulins. These variables can be overcome by the use of labeled albumin.

It is conceivable though unlikely that homologous plasma is metabolized faster in roentgen irradiated animals. If so, any difference in activity of labeled material between roentgen irradiated and normal animals would increase progressively with time; such a relationship, however, was not observed. Thus, it seems probable that the difference between normal and irradiated animals is due to an increased capillary permeability.

*The fate of antigenic material within reticulo-endothelial cells* is not known. After the intravenous injection of $P^{32}$-tagged heterologous red blood cells there is a rapid increase of radiophosphorus in the liver and spleen followed by a rapid decrease to an extent that is likely to go hand-in-hand with destruction of red blood cells. The activity of these organs falls to about 50 per cent of the maximum in 120 minutes. Such a loss can hardly be ascribed to exchange of phosphorus between normal erythrocytes and the surrounding tissue.

In contrast to antigenic red cells, non-antigenic colloidal $Au^{198}$ is accumulated with great rapidity in reticulo-endothelial cells and is retained for weeks in the liver and spleen. It is likely that the colloidal particles adsorb or are adsorbed by plasma proteins before phagocytosis. There are at present no precise procedures for determining the phagocytic ability of macrophages. Radiogold sols would be suitable for this purpose because they are localized almost exclusively in reticulo-endothelial cells were it not for their removal from the circulation so rapidly that it is not possible to distinguish small differences in phagocytic ability. Similar observations were made by Barrow *et al.*[3]

In a few experiments, attempts were made to partially block the reticulo-endothelial system and thereby slow down phagocytosis. The injection of labeled colloid was preceded by that of stable sol, usually 10 to 30 times the original concentration (Table VIII). Again, there was a faster rate of disappearance in roentgen irradiated than in normal rabbits, but the blocking effect was insignificant. It became apparent that in order to decrease the phagocytic rate sufficiently a greater degree of blockage would be required than was feasible with this type of colloid.

In studying the effect of an agent on phagocytosis one may distinguish between phagocytic *capacity* as indicated by the maximum amount of material removed from the circulation by phagocytic cells, and *affinity* of phagocytic cells for foreign particles as indicated by the speed of re-

TABLE VIII

PER CENT* DISAPPEARANCE OF COLLOIDAL $Au^{198}$ FROM THE BLOOD OF NORMAL AND IRRADIATED RABBITS 5 MIN. AFTER INTRAVENOUS INJECTION FOLLOWING NONRADIOACTIVE Au SOL BLOCKAGE

| Days after Irradiation | Blocking† | Normal | Blocking Efficiency | Roentgen Irradiated | Blocking Efficiency | Roentgen Irradiated / Normal |
|---|---|---|---|---|---|---|
| | | | per cent | | per cent | |
| 1 | — | 53.1 | — | 75.4 | — | 1.4 |
| | 30 | 39.0 | −26.5 | 59.1 | −21.6 | 1.5 |
| | 60 | 34.1 | −35.8 | 61.0 | −19.0 | 1.8 |
| 3 | — | 42.0 | — | 78.6 | — | 1.9 |
| | 30 | 47.8 | +11.4 | 70.1 | −10.8 | 1.5 |
| | 60 | 40.7 | − 3.0 | 50.8 | −35.2 | 1.3 |
| 5 | — | 89.5 | — | 82.7 | — | 0.9 |
| | 30 | 78.9 | −11.8 | 81.8 | − 1.0 | 1.0 |
| 5 | — | 69.6 | — | 78.0 | — | 1.1 |
| | 30 | 62.8 | − 9.7 | 82.5 | + 6.0 | 1.3 |
| 8 | — | 73.1 | — | 85.2 | — | 1.2 |
| | 30 | 79.8 | + 9.2 | 87.0 | + 2.1 | 1.1 |
| 8 | — | 83.3 | — | 85.4 | — | 1.0 |
| | 30 | 56.0 | −32.8 | 86.8 | + 1.7 | 1.6 |

* The measured 1 min. value was taken as 100 per cent.
† The ratio of $Au^{197}$ injected for blocking to the $Au^{198}$ injected in the disappearance test.
(Different animals were used for various days after irradiation.)

moval of a small quantity of material introduced.

An extraordinarily high phagocytic affinity is indicated by studies of the disappearance of radioactively labeled colloids from the circulation of man,[19] dogs,[17] and rabbits,[3] showing that within a few minutes after injection most of the activity leaves the circulation according to the exponential law. This phagocytic affinity is not diminished by massive irradiation. Deviations from exponential behavior as time progresses are due to a small residuum which includes particles phagocytosed by circulating white cells[17] and other effects still not well understood. Phagocytic capacity is related to the amount of foreign material required to block the reticulo-endothelial cells. Attempts to demonstrate differences in blocking of normal and roentgen irradiated animals deserve further study.

Since most of the injected material is removed primarily by the liver, it has been suggested that removal of large Au colloids occurs almost completely on one passage through the liver. If this be the case, the rate of removal is governed more by the rate of blood flow through this organ than by affinity of the phagocytic cells for the particles. A variation in the latter parameter would effect only the distribution of the removed material in the organ and not the kinetics of particle disappearance which is controlled by the fraction of the blood volume which traverses the liver per unit time.[17] This discussion points to the complexity of the problems related to *in vitro* tests of phagocytic capacity and affinity. Other factors, such as the rapid regenerative ability of reticulo-endothelial cells and failure of one material to block uptake of another material, are well known. Thus, a final interpretation of the disappearance curves of gold colloids awaits better knowledge of the processes involved.

The experimental data here presented show that physiological and pathological research can be done with great precision in as small an animal as the mouse by semi-micro techniques, utilizing radioisotopes and the gamma-ray ion chamber. Material balance studies using these techniques (Table VII) gave an average recovery of 101.5 per cent with a range of 96.6 to 104.8 per cent.

## SUMMARY AND CONCLUSION

The disappearance rate of labeled homologous and heterologous plasma, homologous and heterologous erythrocytes, Evans blue, and radiogold was studied in rabbits and mice. It was found that one day after irradiation all of these substances disappeared faster from the circulation of roentgen irradiated than from that of normal animals. These results are interpreted, in the light of other observations, as indicating a heightened capillary permeability caused by irradiation.

Phagocytic activity by macrophages is enhanced in roentgen irradiated animals because of greater demand, but phagocytic affinity does not appear to be significantly altered. The extraordinary rapidity of phagocytosis of intravenously injected particles is demonstrated by radioisotope methods. The rapid breakup of foreign erythrocytes within reticulo-endothelial cells is quantitated by measurements of the loss of $P^{32}$ activity from the tagged erythrocytes.

Valuable technical assistance was furnished by Miss Mary M. Knoohuizen, Mr. John J. Lane, and Mr. William D. Gude.

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## REFERENCES

1. Allen, J. G. Progress Report, Abnormal Bleeding. Argonne National Laboratory Report No. 4474, 1950.
2. Allen, T. H., and Orahovats, P. D. Reaction of T-1824 anion and T-1824 albumin with liver slices. *Fed. Proc.*, 1949, *8*, 3.
3. Barrow, J., Tullis, J. L., and Chambers, F. W. Effect of total body x-radiation, antistine and pyribenzamine on the phagocytic function of the reticulo-endothelial system in rabbits injected intravenously with colloidal gold. Naval Med. Research Inst. Report No. 24, Project NM007039, 1949.
4. Bigelow, R. R., Furth, J., Woods, M. C., and Storey, R. H. Endothelial damage by x-rays disclosed by lymph fistula studies. *Proc. Soc. Exper. Biol. & Med.*, 1951, *76*, 734–736.
5. Dunlap, C. E. Effects of radiation on blood and hemopoietic tissues, including spleen, thymus and lymph nodes. *Arch. Path.*, 1942, *34*, 562–608.
6. Fine, J., and Seligman, A. M. Traumatic shock; study of problem of "lost plasma" in hemorrhagic shock by use of radioactive plasma protein. *J. Clin. Investigation*, 1943, *22*, 285–303.
7. Furth, J., Andrews, G. A., Storey, R. H., and Wish, L. Effect of x irradiation on erythrogenesis, plasma and cell volumes. *South. M. J.*, 1951, *44*, 85–92.
8. Gibson, J. C., Jr., and Evans, W. A., Jr. Clinical studies of blood volume; clinical application of method employing azo dye "Evans blue" and spectrophotometer. *J. Clin. Investigation*, 1937, *16*, 301–316.
9. Gofman, J. W. Studies with colloids containing radioisotopes of yttrium, zirconium, columbium, and lanthanum. I. Chemical principles and methods involved in preparation of colloids of yttrium, zirconium, columbium and lanthanum. *J. Lab. & Clin. Med.*, 1949, *34*, 297–304.
10. Goldie, H., and Hahn, P. F. Distribution and effect of colloidal radioactive gold in peritoneal fluid containing free sarcoma 37 cells. *Proc. Soc. Exper. Biol. & Med.*, 1950, *74*, 638–642.
11. Hevesy, G., and Zerahn, K. Determination of red corpuscle content. *Acta physiol. Scandinav.*, 1942, *4*, 376–384.
12. Lange, C., and Harris, A. H. Citrate gold of optimal and reproducible sensitivity for use in colloidal gold reaction; its preparation and control. *Am. J. Pub. Health*, 1944, *34*, 1087–1092.
13. Lowry, O. H., and Bessey, O. A. Adaptation of Beckman spectrophotometer to measurements on minute quantities of biological materials. *J. Biol. Chem.*, 1946, *163*, 633–639.
14. Nieset, R. T., Porter, Blanche, Trautman, W. V., Jr., Bell, R. M., Parson, W., Lyons, C., and Mayerson, H. S. Determination of circulating red blood cell volume with radioactive phosphorus. *Am. J. Physiol.*, 1948, *155*, 226–231.
15. Rawson, R. A., Binding of T-1824 and structurally related diazo dyes by plasma proteins. *Am. J. Physiol.*, 1943, *138*, 708–717.
16. Reeve, E. B. Methods of estimating plasma and total red cell volume. *Nutritional Abstracts and Reviews*, 1948, *17*, 811.
17. Sheppard, C. W., Jordan, G., and Hahn, P. F. Disappearance of isotopically labeled gold colloids from circulation of dog. *Am. J. Physiol.* 1951, *164*, 345–350.
18. Sheppard, C. W., and Martin, W. R. Cation exchange between cells and plasma of mammalian blood. *J. Gen. Physiol.*, 1950, *33*, 703–722.

19. Sheppard, C. W., Wells, E. B., Hahn, P. F., and Goodell, J. P. B. Studies of distribution of intravenously administered colloidal sols of manganese dioxide and gold in human beings and dogs using radioactive isotopes. *J. Lab. & Clin. Med.*, 1947, *32*, 274–286.
20. Simplified ionization chamber. Atomic Energy Commission Isotope Division Circular No. A-7, 1949.
21. Snell, F. D., and Snell, C. T. Colorimetric Methods of Analysis. D. Van Nostrand Company, Inc., New York, 1945, 1, 408.
22. Storey, R. H., Wish, L., and Furth, J. Changes in cell and plasma volumes produced by total body x radiation. *Proc. Soc. Exper. Biol. & Med.*, 1950, *74*, 242–244.
23. Wish, L., Furth, J., and Storey, R. H. Direct determinations of plasma, cell and organ-blood volumes in normal and hypervolemic mice. *Proc. Soc. Exper. Biol. & Med.*, 1950, *74*, 644–648.

# A NEW ROTATION ROENTGEN THERAPY UNIT*†

*By* MORTON M. KLIGERMAN, M.D., *and* HENRY G. SCHAEFER
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ROTATION roentgen therapy is one method of delivering an adequate dose of roentgen radiation to deep-seated tumors without causing undue damage to the skin. By distributing the incident beam over a large area, relatively little effect occurs at any one point on the surface of the body. In effect, this method represents an expansion of the technique of multiple port therapy by cross-firing the tumor through an infinite number of portals.

In 1906, Pohl[6] first suggested the advantages of rotation roentgen therapy. In recent years de Rochemont,[1] Nielsen,[5] Hawley,[4] Hare *et al.*[3] and Green[2] have submitted evidence of its usefulness in solving the problem of delivering a cancerocidal dose of roentgen rays to a lesion situated deep within the body with minimum effects in the skin.

Two methods of rotation roentgen therapy have been employed: (1) rotation of the tube around the immobile patient, and (2) rotation of the patient either erect or horizontal in the fixed beam of roentgen rays. Equipment of the second type must have stability, balance, flexibility, and should be movable if it is to be used in a department or office where the volume of work does not permit a deep therapy room to be used continuously for rotation therapy. The purpose of this communication is to describe an apparatus (Fig. 1) designed for the Radiologic Service of the Presbyterian Hospital which combines these desirable characteristics.

## CHARACTERISTICS

To secure the necessary mobility, the entire unit has been mounted on a steel chassis equipped with rubber casters. It is stored in a corner of the treatment room. When it is to be used it can be rolled into place, centered, and fixed in position for operation within five minutes.

The tumor must be placed at or near the axis of rotation. Yet, stability and balance must be maintained in spite of an eccentrically placed center of gravity in respect to the axis of rotation. This unit was so constructed that no eccentricity of placement of a patient weighing as much as 350 pounds will alter the stability. To

FIG. 1. Sketch of the rotation therapy unit now in use at the Presbyterian Hospital.

* From the Department of Radiology, College of Physicians and Surgeons, Columbia University, and the Radiologic Service of the Presbyterian Hospital, New York.

† Construction of this unit was partially supported by a grant from the Damon Runyon Memorial Fund.

accomplish this, the turntable was made with a diameter of 42 inches, which seems to be the minimum useful size that will permit the eccentric loading described. A ball race is located at the periphery of the turntable for balance. A centrally located steel shaft, 1 inch in diameter, eliminates side-to-side motion.

On this large revolving platform, two trucks are mounted one on top of the other (Fig. 2). They move at right angles to one another. The lower truck permits an extreme lateral excursion of 42 cm., while mounted on top of this the second truck can

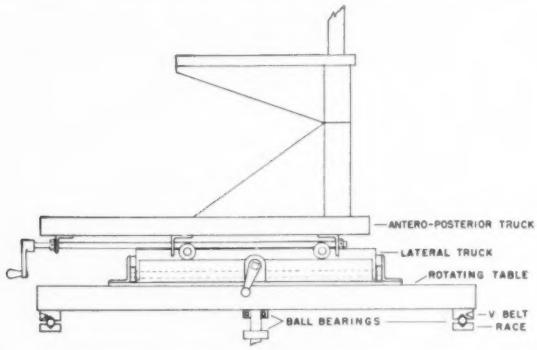


Fig. 2. Diagrammatic detail of the major working parts of the rotation therapy unit drawn to scale from the designer's blueprints.

be moved 26 cm. in an anteroposterior direction. The trucks are positioned by triple threaded rods which are turned with hand cranks. This permits rapid positive centering of the lesion to the central ray of the roentgen-ray beam. Manual operation of these trucks was preferred over a motor drive since devices of the latter type have a great tendency to drift beyond the position desired after the current is turned off.

Patients may be treated either seated or standing, and are held in position by a stanchion which is made of 2 inch pipe. This is held upright in a keyed receptacle mounted on the topmost truck. The same stanchion is used with or without the removable seat. In addition, a special stretcher can be fixed in the same receptacle for rotation of patients in the horizontal position. When this is done, the roentgen-ray beam is angled so that the central ray passes beneath the tumor mass. "By-passing" the tumor in this manner, as described by Green,[2] delivers a relatively homogeneous dose of roentgen radiation to the entire tumor mass.

The clamping devices which immobilize the patient with respect to the stanchion are essentially square, hollow metal bars which can be moved to any height on the stanchion. On each side of the bar are right-angled extensions which are adjusted to the the patient's sides by the single two-handed motion of pushing them along the square bar. They are prevented from moving by a ratchet after this adjustment is made.

### POWER AND CONTROL

The turntable is belt driven by a $\frac{1}{4}$ horsepower electric motor and reduction gear. In order to permit instantaneous reversal, a motor was selected which operates on 220 volt, three phase current. The belt extends from the motor pulley around the circumference of the metal ball race of the turntable. By varying the size of the motor pulley, the speed of rotation can be varied. We have chosen a speed of 2.3 revolutions per minute. This is fairly rapid, but no patient has yet complained of dizziness or any other discomfort from this rate of circular travel.

The rotation unit can operate in continuous circular motion, or it can be made to turn back and forth through any desired arc. This is automatically and remotely controlled from without the treatment room by a slave-master selsyn motor arrangement. When the micro-switch activators on the control panel are set to the desired number of degrees, the turntable will travel back and forth through this arc.

In the construction of the rotation roentgen therapy unit,* all possible materials and parts were of stock sizes. This greatly reduced the cost of the apparatus and minimizes any future spare part problem.

* This unit was built by the Gobe Engineering and Repair Works, 1001 Saw Mill River Road, Yonkers, New York.

## SUMMARY AND CONCLUSION

A new rotation roentgen therapy unit has been described which can be adapted to any type of roentgen treatment machine.

At the time this is written, the rotation therapy unit has been in operation seven months. It has met all the requirements of stability, balance, flexibility and mobility. It has been simple to operate, and over the period of observation has thus far been free of operational failures.

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## REFERENCES

1. du Mesnil de Rochemont, R. Die Dosierungsgrundlagen der Rotationsbestrahlung. *Strahlentherapie*, 1937, *60*, 648–674.
2. Green, A. Rotation roentgen therapy in horizontal plane; general considerations and clinical aspect. *Acta radiol.*, 1949, *31*, 273–284.
3. Hare, H. F., Lippincott, S. W., Jr., Sawyer, D., Trump, J. G., Webster, E. W., Wright, K. A., Evans, W. W., and Granke, R. C. Physical and clinical aspects of supervoltage rotational therapy. *Radiology*, 1951, *57*, 157–168.
4. Hawley, S. J. Rotation therapy: theory and clinical applications. *Radiology*, 1948, *51*, 205–213.
5. Nielsen, J. Clinical results with rotation therapy in cancer of esophagus. *Acta radiol.*, 1945, *26*, 361–389.
6. Pohl. Quoted by Myer, H. Das Problem der Druesfeuerwirkung in der gynaekologischen Röntgentherapie. *Zentralbl. f. Gynäk.*, 1913, *37*, 1741–1752.

# LOCALIZATION OF THE GALLBLADDER

## A NEW TECHNIQUE

*By* LEVAN MADDOX, R.T.*

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THROUGH improved drugs better diagnostic cholecystograms are being made. The propionic acid group of dyes (priodax) are far easier on the patient than the tetraiodophenolphthalein compouuds. It follows that better roentgenograms can be, and are, expected. Priodax is excreted mainly by the kidneys and there is no dye in the colon to interfere with the gallbladder shadow. This is in contrast to tetraiodophenolphthalein, which was also found in the colon and occasionally obscured the gallbladder.[1]

The necessity of obtaining the best centered and the sharpest possible roentgenograms in this examination has been repeatedly stressed but bears frequent repetition. Proper density, maximum detail and a minimum of motion are essential, especially in the poorly functioning gallbladders where the lack of dye makes visualization of the cholesterol stones difficult.

In this paper a further refinement in technique is offered for sharper and more accurately localized demonstration of the gallbladder and adjacent structures. Following localization of the desired target on the survey roentgenogram, a smaller, more detailed and contrasting spot roentgenogram can be made.

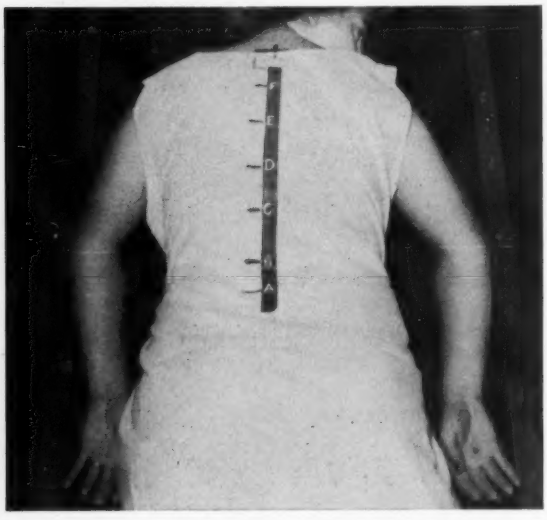


FIG. 1. Routine survey roentgenogram showing localizing tape in position with all markings.

Review of the literature reveals numerous articles on this subject, all with the same intent; but many techniques seem too cumbersome and less accurate than the method here described. Whelan[4] and Kent[2] have presented techniques for localization which seem to have such faults. Standard texts of roentgenographic techniques seem much less precise in this field than in most other regional studies. This apparent inexact technique can be understood when it is realized that the gallbladder may appear vertically anywhere from the ninth rib to the true pelvis and laterally from a point overlapping the spine to the right abdominal wall. In addition to the variation in position peculiar to the type or habitus of the subject, the gallbladder undergoes some displacement with change of posture from prone to supine, to erect or lateral positions.[3] Finally, during inspiration, it moves down and toward the midline. It is because of these unpredictable variants that the following technique has been evolved.

The localization device used here is a 30 centimeter narrow adhesive strip with six small lead letters attached and spaced at 5 cm. intervals. When making the usual survey roentgenogram, this tape is placed along the spinous processes of the area that is usually exposed when making such a film. The location of each of the lead letters is marked on the gown or skin with a skin pencil (Fig. 1).

Where an open-back gown is not used for female patients, the survey roentgenogram

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is made in the same manner as previously described except that the location of the lead letters will be marked on the gown. The neck line of this gown should be marked on the skin to insure the same position for subsequent spot roentgenograms. This gown is marked with the patient's initial for use of the same person when the study is made after the fat meal.

The survey film is developed immediately and the exact position of the gallbladder can be determined by its relation to the nearest lead letter and by the distance of the gallbladder from the spinous process (Fig. 2).

All subsequent roentgenograms can be coned down to any desired size by referring only to the skin or gown marks corresponding to the desired target (Fig. 3).

The advantages of this technique are:

1. Its simplicity decreases the time for the gallbaldder study.

2. A decrease in the number of films necessary to make a satisfactory examination, and economy is also achieved by the negligible cost of the localizing device.

Fig. 2. Survey roentgenogram showing relation of gallbladder to lead letters.

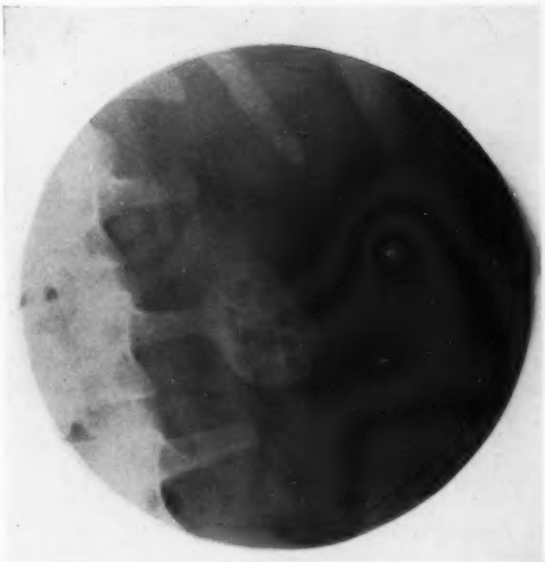

Fig. 3. Final close definition study made possible by the localizing device.

3. Because of the ability to accurately localize the shadow in question, repeat studies can be improved by accurate coning and focusing.

4. Improved spot localization of any desired region of the chest or abdomen can be obtained by similar use of this device.

5. It gives the technician self assurance and helps him to produce an examination of superior quality.

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REFERENCES

1. Dannenberg, M. Cholecystographic studies with priodax. Am. J. Roentgenol. & Rad. Therapy, 1944, *51*, 328–335.

2. Kent, Thelma. Gall-bladder radiography: table of positions based on two measurements. *X-Ray Technician*, 1944, *16*, 101–107.

3. Merrill, Vinita. Atlas of Roentgenographic Positions. C. V. Mosby Company, St. Louis, 1949.

4. Whelan, F. J. Technique for locating areas on scout roentgenogram by means of co-ordinating charts. *X-Ray Technician*, 1946, *17*, 471–474.

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*Published by:* Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois.

*Issued monthly. Annual subscription: United States, Mexico, Cuba, Central and South America, $15.00; Canada, $16.00; other countries, $17.00. Current single numbers, $1.50. Advertising rates submitted on application. Editorial office, 110 Professional Building, Detroit 1, Michigan. Office of publication, 301–327 East Lawrence Avenue, Springfield, Illinois. Information of interest to authors and readers will be found on page iv.*


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*Editor:* Lawrence Reynolds, 110 Professional Building, Detroit 1, Mich.

*Assistant Editor:* Ruth Bigelow, 110 Professional Building, Detroit 1, Mich.

*Fifty-third Annual Meeting:* Shamrock Hotel, Houston, Texas, September 23, 24, 25 and 26, 1952.

### AMERICAN RADIUM SOCIETY

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*Thirty-fourth Annual Meeting:* Stevens Hotel, Chicago, Ill., June 8, 9 and 10, 1952.

# EDITORIALS

## UNEXPECTED SOURCES OF STRAY ROENTGEN RADIATION

THERE has been a tremendous growth during the past decade in the science of electronics. Devices, instruments and apparatus of many types are now in current use in which a certain electron beam is propelled forward in an evacuated tube by an accelerating potential. The situation is often very similar to that encountered in a roentgen tube except that the metallic "target" upon which the accelerated electron beam impinges is usually replaced by a fluorescent screen, the kinetic energy of the electron beam being transformed into the fluorescence of the material used to cover the surface of the screen. In the thermionic valve tube the electrons emitted by the cathode serve to carry the current in the rectified direction.

It is obvious that in this process either the screen, or the metal anode, or the beam-forming accessories may constitute under certain circumstances potential or actual sources of stray roentgen radiation. If no protection is provided, unsuspected exposure may be received, not only by the personnel working in the immediate vicinity of the apparatus but also by others at some distance away, depending on the quality and thus the penetration of the roentgen rays produced.

Of the several electron beam apparatus which may come into consideration from the point of view of emission of stray roentgen radiation, three are of particular interest because of their wide use in the medical field: the electron microscope, the cathode-ray oscillograph and the thermionic valve tube.

As regards the electron microscope, it was suspected early that the observer viewing the fluorescent screen might be exposed to radiation levels which are definitely hazardous. Hillier and Ellis[1] found that when a very large condenser aperture was used or when the condenser aperture assembly was removed to focus at low magnification, a relatively large fraction of the electron beam reached the fluorescent screen, resulting in production of roentgen rays in quantities above the accepted tolerance dose. Therefore, they recommended that the roentgen-ray output be measured and guarded against whenever a condenser aperture greater than the standard aperture is used. Silverman, Elliott and Greenfield[2] in making a general radiation survey of a physical plant noted, however, that radiation well above background levels existed at all times in the vicinity of a 50 kv. electron microscope used in their laboratory, and that roentgen rays were produced continuously by various metal parts of the beam-forming accessories acting as targets to the accelerated electrons. These authors carried out a series of measurements with the aid of a calibrated dosimeter on the instrument itself. They found that the average dose at the top port was approximately 1,500 milliroentgens per hour and at the intermediate viewing port 70 mr per hour. Since the authors permit in their laboratory a maximum dose of only 50 mr per day a person engaged in a full day's work would receive under these circumstances several hundred times the maximum permissible exposure. Quality determinations showed the emerging roentgen rays to have a wavelength

[1] Hillier, James C., and Ellis, S. G. The illuminating system of the electron microscope. *J. Appl. Phys.*, 1949, *20*, 700–706.

[2] Silverman, Louis B., Elliott, Sylvia B., and Greenfield, M. A. Radiation survey of x-ray output of an electron microscope from personnel hazard viewpoint. *Science*, 1949, *110*, 376–377.

range of 0.45 to 0.50 Ångström units and a half-value layer of 1.0 to 1.7 mm. of aluminum corresponding to the peak energy of a continuous roentgen-ray spectrum arising from 50 kv. electrons. If the ordinary glass of the viewing ports was replaced by ¼ inch thick lead glass, the roentgen-ray emission at the ports was reduced to less than 1 mr per hour. Silverman, Elliott and Greenfield state that ordinary glass instead of lead glass was used accidentally by the manufacturer in the instrument analyzed by them.

Watson and Preuss[3] surveyed three electron microscopes operating under normal conditions, as well as under abnormal conditions, when, for example, motion pictures are taken of certain specimens. The abnormal conditions referred to include the tilting of the final viewing screen to an angle of about 30 degrees and the replacing of the standard condenser aperture of 25 mils with one of 50 mils. These authors found that under normal conditions the roentgen emission at the top port, where it usually assumes the greatest value, was apparently eliminated by supplying the microscopes with lead glass. The intermediate and final ports, however, were not completely protected, although it was felt that the operator, unless he worked for unusually long periods or was constantly closer than 3 inches, would receive exposure within tolerance limits. Under abnormal conditions very high dose rates were recorded. At 1 inch distance from the microscope window, the roentgen-ray output amounted to 45 mr per hour, so that, if an observer should spend six hours at this position while focusing, he would receive in that short period of time practically the entire amount of 0.3 r now accepted as the maximum permissible exposure for a whole week. Prolonged work under such conditions undoubtedly would produce injury to the eyes leading to probable cataract formation.

Recently, Larks[4] conducted a more comprehensive survey study from the point of view of the industrial hygienist with the aim of localizing possible sources of stray roentgen rays in a number of electron beam devices. For the measurement of the roentgen rays emitted by an electron microscope, he used the Geiger-Müller counter and the photographic method. He, too, found that the largest amount of radiation emerged from the lower port when the viewing screen was tilted about 30 degrees. Under this condition, he obtained a value of 12 mr per hour which, although somewhat lower than that recorded by Watson and Preuss, is still considerably above the accepted tolerance level. At the other ports the radiation appeared to be of the order of magnitude of the tolerance dose, or about 6 mr per hour.

The electron beam of the cathode-ray tube is practically devoid of inertia and therefore ideally suited to studying variations in electrical potential. On this principle are based many types of oscillographs, oscilloscopes and synchroscopes employed for industrial investigations. Several of them are used with advantage also for the study of radiologic problems and a few are now finding applicability in the general medical field. The latest example is a cathode-ray oscillograph adapted to the more accurate registration of electrocardiographic patterns.[5] Larks[4] surveyed an industrial electron beam oscillograph and already on preliminary investigation found that the entire area surrounding the instrument exhibited a radiation level which was many times that of the normal background. On further study, he noted that the greatest roentgen-ray emission occurred in the vicinity of the

[3] Watson, John H. L., and Preuss, Luther E. X-radiation from electron microscopes. *Science*, 1950, *112*, 407–409; also, Preuss, Luther E., and Watson, John H. L. A technique for taking motion pictures of electron microscope images. *J. Appl. Phys.*, 1950, *21*, 902–903.

[4] Larks, S. D. Stray x-rays from electron beam instruments and some biological implications. *Am. Indust. Hyg. Assoc. Quart.*, Dec. 1951, *12*, No. 4; also, Larks, S. D. X-radiation from television picture tubes and other cathode ray tubes. Unpublished thesis. Northwestern University, 1951.

[5] Langner, Paul H. The value of high fidelity electrocardiography using the cathode ray oscillograph and an expanded time scale. *Circulation*, Feb., 1952, *5*, 249–256.

electron gun, particularly through several rectangular openings of the metal housing, and at the glass wall of the discharge tube. Quantitometric determinations, made with the aid of the Victoreen ionization chamber and the photographic method, revealed that in the immediate vicinity of the electron gun and discharge tube the radiation was of the order of 1 roentgen in three hours and at the rectangular openings of the metal housing of the order of 1.5 to 2 r in three hours. These amounts represent values which even at a distance of 3 feet from the instrument are considerably above the permissible dose of 6.25 mr per hour, or 0.3 r per week. A sheet of $\frac{1}{8}$ inch lead placed across one of the rectangular openings has greatly reduced but not completely eliminated the emergent radiation, indicating that a harder component must also be present in the beam.

A third source of possible stray roentgen radiation, of direct interest to the radiologist, is the thermionic valve tube. The first observations in this regard were made at the very start of replacing mechanical rectification with thermionic valve tube rectification in the roentgen-ray generating apparatus. Thus Bromley[6] in 1929 published five roentgenograms of a hand which were made with a seven second exposure at a distance of 30 inches from a thermionic valve tube used for rectification in a 60 kv., 30 ma. set. There was no roentgen-ray emission during the first minute while the valve tube was still cold, but after heating the valve filament continuously for five minutes the roentgen radiation which emanated from the transformer cabinet containing the thermionic valve tube was sufficiently strong to permit the taking of a reasonably good roentgenogram of the hand or the roentgenoscopic examination of the chest in a darkened room.

This large roentgen-ray emission by the thermionic valve tubes of the early days, when many unsolved technical problems confronted the manufacturers, is easily understandable. Fundamentally, there is no essential physical difference between the thermionic valve tube and the ordinary roentgen tube. Both are vacuum tubes, containing a hot filament cathode and a cold metal anode. However, the construction of the thermionic valve tube must be such that very little voltage drop occurs between the electrodes and therefore the electrons impinge upon the anode with an energy which is insufficient to produce roentgen rays. This is accomplished by operating the roentgen tube near its saturation value while the thermionic valve tube is so adjusted that the maximum current is less than saturation current. Bell[7] has shown that if the maximum momentary current passing through a thermionic valve tube approaches very near to the saturation value, the valve tube becomes at once dangerous, because it emits roentgen rays, and inefficient, because there is a large drop of voltage across it. Wright[8] performed the following interesting experiment: he passed current through a thermionic valve tube until it emitted roentgen rays, then without altering anything else he increased the temperature of the filament and the emission ceased; again he increased the high tension current and again roentgen rays were emitted; and so on, until the experiment came to an end with the burning out of the filament. In analyzing the relationship of the saturation currents of the valve tubes and roentgen tube to each other, Wright found that to avoid the danger of emission of roentgen rays from the valve tubes the saturation current of the roentgen tube must always be less than that of any of the valve tubes.

During the two decades following these observations, the enormous progress made in the construction of roentgen apparatus of all kinds has brought with it such a technical perfection of the thermionic valve tube that we have long ceased to consider it as a source of possible danger.

[6] Bromley, J. F. Note on the x-ray emission from thermionic valves. *Brit. J. Radiol.*, 1929, *2*, 587.

[7] Bell, G. Eric. The emission of x rays by rectifying valves. *Brit. J. Radiol.*, 1930, *3*, 364–368.

[8] Wright, R. S. Thermionic rectification of x-ray circuits. *Brit. J. Radiol.*, 1930, *3*, 369–374.

It is therefore of considerable interest that Ellis and Clark[9] very recently called attention to the fact that under certain circumstances a hazard may exist which should not be ignored. These authors, in experimenting with constant potential roentgen therapy units, noted that roentgen rays may be emitted from thermionic valve tubes even when operating under normal conditions; that is, with the maximum filament voltage specified by the manufacturers. They found that the amount of radiation emanating from the cathode assembly of the valve varies with the type of valve and in a given case diminishes with time during the constant daily operation of the apparatus. On inquiry, they further found that this phenomenon is little known, and therefore merits recording.

Ellis and Clark studied the intensity and quality of the roentgen rays thus emitted. Using a condenser ionization chamber, suitably shielded with lead from the scattered radiation, they found a maximum intensity of 0.32 r per hour at a distance of 1 meter from the valve tube, or 38 times the maximum permissible dose of 0.3 r per week for a thirty-five hour week. As already stated, the output diminished with the time of continuous operation of the valve tube but returned to its initial value after rest over night. The determination of the quality of the roentgen rays, which, owing to the variation in output, was rather difficult to perform, yielded a soft component of 2.3 mm. Al half-value layer and a hard component of 1.0 mm. Cu half-value layer, corresponding to an effective wavelength of 0.413 and 0.153 Ångström unit respectively.

Ellis and Clark express the opinion that the cathode assembly of the thermionic valve tube emits the stray roentgen rays during the inverse cycle, when the voltage across the valve varies from zero to approximately the voltage across the roentgen tube. They state that the thermionic valve tube, for which the above figures are quoted, had a life of 3,360 hours when the filament became broken.

It is clearly evident from the aforementioned observations that an incessant vigilance is necessary when working with any type of electron beam instrument or device. For the electron microscope and cathode tube oscillograph, Larks[4] proposes the following safety recommendations: that lead shielding be used around the electron area; that the plate glass in the vicinity of the critical areas be replaced by lead glass; that an obligatory survey be carried out whenever installing such an instrument; and that a health physics program be instituted for the operating personnel. The same recommendations can be applied to any similar electron beam instrument. The rules for the medical protection against stray radiation emitted by roentgen apparatus are well known.[10] Ellis and Clark[9] advise than when using equipment with unshielded thermionic valve tubes and when the valve tubes are located in the treatment room, the voltage operating across the roentgen tube be considerably reduced or preferably switched off while the patient is being set up by the staff for treatment. It may be mentioned that this recommendation is already incorporated in the standard safety rules[10] but its reiteration is important in view of the fact that several newer installations are supplied with an automatic lead shutter of the otherwise shielded roentgen tube, thus creating a sense of false security when the possible exposure from the thermionic valve tubes is not taken into consideration.

T. Leucutia, M.D.

[9] Ellis, R. E., and Clark, L. H. S. A potential source of danger: the emission of x rays from rectifying valves in x-ray therapy units. *Brit. J. Radiol.*, Jan., 1952, *25*, 17–18.

[10] Medical x-ray protection up to two million volts. Handbook 41. U. S. Department of Commerce, National Bureau of Standards. March 30, 1949.

# ROBERT JOHN MAY

## 1879–1951

DR. ROBERT JOHN MAY, of Cleveland, Ohio, a member of the American Roentgen Ray Society since 1926, died suddenly on October 17, 1951, presumably of a heart attack, while driving his automobile to his office.

Dr. May was born in 1879 in Westlake, Ohio, a suburb of Cleveland. At the time of his death he resided in Lakewood, not far from his birthplace. He graduated in 1906 from Western Reserve University School of Medicine and served an internship at Cleveland General Hospital, then conducted a general practice in Cleveland.

He took post-graduate work in the Department of Radiology of the General Hospital, Vienna, Austria, in 1913–1914. In 1915 he became head of the Department of Roentgenology of St. Luke's Hospital, Cleveland; he resigned in 1947 to enter private practice.

Dr. May was a member of the following scientific societies: Cleveland Academy of Medicine, Ohio State Medical Association, American Medical Association, Ohio State Radiological Society, Cleveland Radiological Society (charter member, President 1932), diplomate of the American Board of Radiology, 1934; Fellow of the American College of Radiology; member of the American Roentgen Ray Society, 1926; Radiological Society of North America, serving on its Executive Committee 1921–1924, as Secretary-Treasurer 1926–1928, President-elect 1929, and President 1930.

Dr. May's brother, Dr. Raymond V. May, who died in 1946, was associated with him in the practice of roentgenology from 1920.

Bob was a genial fellow and competent in his medical specialty. The confidence of his colleagues in his administrative ability is testified by his election to several offices in radiological societies which he conducted proficiently.

U. V. Portmann, M.D.

# SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

## MEETINGS OF ROENTGEN SOCIETIES*

### United States of America

**American Roentgen Ray Society**
*Secretary*, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Shamrock Hotel, Houston, Texas, September 23, 24, 25 and 26, 1952.

**American Radium Society**
*Secretary*, Dr. J. E. Wirth, 635 Herkimer St., Pasadena 1, Calif. Annual meeting: Stevens Hotel, Chicago, Ill., June 8, 9 and 10, 1952.

**Radiological Society of North America**
*Secretary*, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y.

**American College of Radiology**
*Executive Secretary*, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois.

**Section on Radiology, American Medical Association**
*Secretary*, Dr. T. Leucutia, Harper Hospital, Detroit 1, Mich. Annual meeting: Chicago, Ill., June 9–13, 1952.

**Alabama Radiological Society**
*Secretary*, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

**Arizona Radiological Society**
*Secretary*, Dr. R. Lee Foster, 507 Professional Building, Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

**Arkansas Radiological Society**
*Secretary*, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

**Atlanta Radiological Society**
*Secretary*, Dr. J. D. King, 35 Linden Ave., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

**Brooklyn Roentgen Ray Society**
*Secretary*, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, October through April.

**Buffalo Radiological Society**
*Secretary*, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

**Central New York Roentgen Ray Society**
*Secretary*, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

**Central Ohio Radiological Society**
*Secretary*, Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

**Chicago Roentgen Society**
*Secretary*, Dr. B. D. Braun, 6 N. Michigan Ave., Chicago 2, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

**Cleveland Radiological Society**
*Secretary*, Dr. Mortimer Lubert, 10515 Carnegie Ave., Cleveland 6, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

**Colorado Radiological Society**
*Secretary*, Dr. W. P. Stampfli, 1933 Pearl St., Denver, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

**Connecticut Valley Radiologic Society**
*Secretary*, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday October and April.

**Dallas-Fort Worth Roentgen Study Club**
*Secretary*, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

**Detroit Roentgen Ray and Radium Society**
*Secretary*, Dr. J. C. Cook, Harper Hospital, Detroit, Mich. Meets monthly first Thursday, October to May, at Wayne County Medical Society Building.

**East Bay Roentgen Society**
*Secretary*, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

**Florida Radiological Society**
*Secretary*, Dr. Nelson T. Pearson, 1109 Huntington Bldg., Miami, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

**Georgia Radiological Society**
*Secretary*, Dr. R. C. Pendergrass, Americus, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

**Greater Miami Radiological Society**
*Secretary*, Dr. Maurice Greenfield, Ingraham Bldg., Miami, Fla. Meets third Wednesday of each month at Veterans Administration Building.

**Houston Radiological Society**
*Secretary*, Dr. F. M. Windrow, 1205 Hermann Professional Bldg., Houston, Texas. Meets fourth Monday each month.

**Illinois Radiological Society**
*Secretary*, Dr. Stephen L. Casper, 1101 Maine St., Quincy, Ill. Meets three times a year.

**Indiana Roentgen Society**
*Secretary*, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

**Iowa X-Ray Club**
*Secretary*, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society.

**Kansas Radiological Society**
*Secretary*, Dr. Charles M. White, 3244 E. Douglas, Wichita 8, Kan. Meets annually with State Medical Society.

**Kentucky Radiological Society**
*Secretary*, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

**Kings County Radiological Society**
*Secretary*, Dr. Marcus Wiener, 1430 48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

**Los Angeles Radiological Society**
*Secretary*, Dr. John B. Hamilton, 210 N. Central Ave., Glendale 3, Calif. Meets second Wednesday each month at Los Angeles County Medical Association Building.

**Louisiana Radiological Society**
*Secretary*, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

**Maine Radiological Society**
*Secretary*, Dr. C. F. Miller, Central Maine General Hospital, Lewiston, Maine.

**Miami Valley Radiological Society**
*Secretary*, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

* Secretaries of societies are requested to send timely information promptly to the Editor.

Michigan Association of Roentgenologists
*President*, Dr. Horace W. Porter, 505 Wildwood Ave., Jackson, Mich.

Mid-Hudson Radiological Society
*Secretary*, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, September to May.

Milwaukee Roentgen Ray Society
*Secretary*, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
*Secretary*, Dr. L. A. Nash, 572 Lowry Medical Arts Bldg., St. Paul 2, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

Mississippi Radiological Society
*Secretary*, Dr. John W. Evans, 621 High Street, Jackson 2, Miss. Meets third Thursday of each month at the Rotisserie Restaurant at 6:30 P.M.

Nebraska Radiological Society
*Secretary*, Dr. R. W. Blanchard, 1216 Medical Arts Bldg., Omaha, Nebr. Meets fourth Thursday of each month at 6 P.M. at Omaha or Lincoln.

New England Roentgen Ray Society
*Secretary*, Dr. L. L. Robbins, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Harvard Club.

New Hampshire Roentgen Ray Society
*Secretary*, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

New York Roentgen Society
*Secretary*, Dr. Irving Schwartz, 45 E. 66th St., New York 21, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

North Carolina Radiological Society
*Secretary*, Dr. J. E. Hemphill, 1420 E. Fifth St., Charlotte 4, N. C. Meets in May and October.

North Dakota Radiological Society
*Secretary*, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings by announcement.

Northeastern New York Radiological Society
*Secretary*, Dr. John F. Roach, Albany Hospital, Albany, N. Y. Meets on the second Wednesday of October, November and March at the University Club, Albany. Annual meeting in June to be announced.

Northern California Radiological Club
*Secretary*, Dr. G. A. Fricker, Sacramento County Hospital, Sacramento, Calif. Meets at dinner last Monday, every second month, except June, July and August.

Ohio State Radiological Society
*Secretary*, Dr. Willis S. Peck, 2001 Collingwood Blvd., Toledo, Ohio. Annual meeting: Mansfield-Leland Hotel, Mansfield, Ohio, May 24 and 25, 1952.

Oklahoma State Radiological Society
*Secretary*, Dr. W. E. Brown, 2020 S. Xanthus, Tulsa 4, Okla. Three regular meetings annually.

Oregon Radiological Society
*Secretary*, Dr. J. Richard Raines, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets monthly from October to June on the second Wednesday of each month at 8:00 P.M. at the University Club.

Orleans Parish Radiological Society
*Secretary*, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

Pacific Northwest Radiological Society
*Secretary*, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

Pacific Roentgen Society
*Secretary*, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
*Secretary*, Dr. J. M. Converse, 416 Pine St., Williamsport. Annual meeting: Bedford Springs Hotel, Bedford, Pa., May 16 and 17, 1952.

Philadelphia Roentgen Ray Society
*Secretary*, Dr. G. P. Keefer, American Oncologic Hospital, Philadelphia 4, Pa. Meets first Thursday each Month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

Pittsburgh Roentgen Society
*Secretary*, Dr. E. J. Euphrat, 3500 Fifth Ave., Pittsburgh 13, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

Radiological Section, Baltimore Medical Society
*Secretary*, Dr. Richard B. Hanchett, 705–6 Medical Arts Bldg., Baltimore, Md. Meets third Tuesday each month, September to May.

Radiological Section, Connecticut Medical Society
*Secretary*, Dr. Fred. Zaff, 135 Whitney Ave., New Haven, Conn. Meets bimonthly on second Wednesday.

Radiological Section, Medical Society of the District of Columbia
*Secretary*, Dr. U. V. Wilcox, 915 Nineteenth St., N. W., Washington 6, D. C. Meets Medical Society Library, third Thursday of January, March, May and October at 8:00 P.M.

Radiological Section, Southern Medical Association
*Secretary*, Dr. Roy G. Giles, Temple, Texas.

Radiological Society of Greater Cincinnati
*Secretary*, Dr. Lee S. Rosenberg, Jewish Hospital, Cincinnati 29, Ohio. Meets first Monday each month, October through May.

Radiological Society of Kansas City
*Secretary*, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Radiological Society of New Jersey
*Secretary*, Dr. Nicholas G. Demy, 912 Prospect Avenue, Plainfield, N. J. Meets annually at Atlantic City at time of State Medical Society and mid-winter at Elizabeth, N. J.

Richmond County Radiological Society
*Secretary*, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga.

Rochester Roentgen Ray Society, Rochester, N. Y.
*Secretary*, Dr. George Gamsu, 191 S. Goodman St., Rochester, N. Y. Meets monthly on last Monday from September through May, 8:00 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
*Secretary*, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr.

St. Louis Society of Radiologists
*Secretary*, Dr. Francis O. Trotter, Jr., 634 N. Grand Blvd., St. Louis 3, Mo. Meets fourth Wednesday each month, except June, July, August and September.

San Diego Radiological Society
*Secretary*, Dr. Rex Uncapher, 7720 Girard Ave., La Jolla, Calif. Meets first Wednesday of each month at the University Club.

San Francisco Radiological Society
*Secretary*, Dr. I. J. Miller, 2680 Ocean Avenue, San Francisco 27, Calif. Meets quarterly.

Section on Radiology, California Medical Association
*Secretary*, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

Section on Radiology, Illinois State Medical Society
*Secretary*, Dr. Harold L. Shinall, St. Joseph's Hospital, Bloomington, Ill.

Shreveport Radiological Club
*Secretary*, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Bay Radiological Society
*Secretary*, Dr. Ford Shepherd, 526 Soquel Avenue, Santa Cruz, Calif. Meets second Wednesday each month.

South Carolina X-Ray Society
*Secretary*, Dr. Henry E. Plenge, Spartanburg General Hospital, Spartanburg, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

Tennessee Radiological Society
*Secretary*, Dr. J. M. Frère, Newell Hospital, Chattanooga,

Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
*Secretary*, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Next meeting: San Antonio, Texas, January 23 and 24, 1953.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 p.m. at University Hospital.

University of Wisconsin Radiological Conference
*Secretary*, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 p.m., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

Utah State Radiological Society
*Secretary*, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
*Secretary*, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
*Secretary*, Dr. John N. Burkey, 555 Medical-Dental Bldg., Seattle 1, Wash. Meets fourth Monday of each month from September through May.

Westchester Radiological Society
*Secretary*, Dr. Walter J. Brown, Northern Westchester Hospital, Mt. Kisco, N. Y. Meets on third Tuesdays of January and October and on two other dates to be announced.

Wisconsin Radiological Society
*Secretary*, Dr. Irving I. Cowan, 425 E. Wisconsin Ave., Milwaukee 2, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-Ray Study Club of San Francisco
*Secretary*, Dr. Charles E. Duisenberg, Palo Alto Clinic, 300 Homer Ave., Palo Alto, Calif. Meets third Thursday at 7:45 p.m., January to June, Lane Hall, Stanford University Hospital; July to December, San Francisco Hospital.

### Cuba, Mexico and Central America

Sociedad de Radiología y Fisioterapia de Cuba
*President*, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Sociedad Mexicana de Radiologia y Fisioterapia
*General Secretary*, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

Sociedad Radiológica Panameña
*Secretary*, Dr. L. Arrieta Sanchez, Apartado No. 86, Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

### British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 p.m.
Medical Members' meeting, on third Friday in each month at 5:00 p.m., 32 Welbeck St., London, W 1.

Faculty of Radiologists
*Honorary Secretary*, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 p.m. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
*Honorary Secretary-Treasurer*, Dr. Jean Bouchard, Suite 305, 1555 Summerhill Avenue, Montreal 26, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
*Secretary*, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electrologie et de Radiologie Médicales
*Secretary*, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

Australian and New Zealand Association of Radiologists
*Honorary Secretary*, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
*Honorary Secretaries*, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. L. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. R. deG. Burnard, 170 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179 B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

### South America

Asociacion Argentina de Radiologia
*Secretary*, Dr. Lidio G. Mocsa, Avda. Gral Paz 151, Córdoba, Argentina. Meetings held monthly.

Sociedad Argentina de Radiologia, Junta Central, Buenos Aires
*Secretary*, Dr. Oscar F. Noguera, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Argentina de Radiologia, Filial del Litoral, Sede, Rosario
*President*, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 19 ha 663 Italia St., Rosario, Santa Fe.

Sociedad Argentina de Radiologia, Filial del Sur, Sede, La Plata
*President*, Prof. Dr. Jose P. Uslenghi, La Plata. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Centro, Sede, Cordoba
*President*, Prof. Dr. David L. Caro, Corro 86, Cordoba. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Norte, Sede, Tucuman
*President*, Dr. Julio Mendez Valladares, Rivadavia 358, Tucuman. Meets monthly.

Sociedad Argentina de Radiologia, Filial de Cuyo Sede, Mendoza.
*President*, Dr. J. A. Orfila, Hospital Central, Mendoza. Meets monthly.

Sociedade Brasileira de Radiologia Medica
*Secretary*, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
*Secretary*, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 p.m. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Colombiana de Radiologia
*Secretary*, Dr. Alberto Torres Focke, Av. 34, No. 17–34, Bogota, Colombia. Meets last Wednesday of each month.

Sociedad Peruana de Radiologia
*Secretary*, Dr. Julio Bedoya Paredes, Apartado 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
*Secretary*, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

### Continental Europe

Société Belge de Radiologie
*General Secretary*, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Société Française d'Electro-Radiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord
*Secretary-General*, Dr. A. Dariaux, 9 bis, Boulevard Rochechouart, Paris IX•, France.

Ceskoslovensk společnost pro rëntgenologii a Radiologii v Praze
*Secretary*, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
*Secretary*, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland.

Gdansk Section, Polish Society of Radiology
*Secretary*, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10:30, X-Ray Dept., Akademia Gdansk.

Warsaw Section, Polish Society of Radiology
*Secretary*, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

Societatea Romana de Radiologie si Electrologie
*Secretary*, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
*Secretaries*, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
*Secretary*, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
*Secretary*, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

Deutsche Roentgen-Gesellschaft
*Secretary*, Dr. Peter Kröker, (22a) Essen-Helsingen, Westpreussenstrasse 21. Meets annually in different towns.

Societa Italiana dr Radiologia Medica
*Secretary*, Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

### India

Indian Radiological Association
*Secretary*, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

## FOURTH INTER-AMERICAN CONGRESS OF RADIOLOGY

The Fourth Inter-American Congress of Radiology will be held in Mexico City on November 2–8, 1952. The Sociedad Mexicana De Radiologia is the host to the Congress and Dr. Manuel F. Madrazo is President. The address of the headquarters of the Congress is Londres No. 13, Mexico City 6, D. F.

The Program Committee has selected two official subjects for this Congress: (1) Radiological Diagnosis of Intraabdominal Tumors, Other Than Gastrointestinal; (2) Radiotherapy of Lymphoblastomas (Lymphosarcoma, Hodgkin's Disease, Leukemias). However, the program will not be limited to these two subjects. The Program Committee extends an invitation to the radiologists of the United States to offer papers on any topic. Twenty minutes will be allowed for each presentation. The titles and an abstract of the material to be presented in the paper should be sent to Dr. James T. Case, Chairman of the American Delegation to the Fourth Inter-American Congress of Radiology, 2315 Bath Street, Santa Barbara, California. The complete text of the paper must be in his hands not later than June 30, 1952.

The registration fee for Regular Members is $24.00, and for Associate Members which include members of the families of the Regular Members is $12.00. The registration fee should be sent to Dr. Baudelio Villanueva, Londres No. 13, Mexico City 6, D. F., before August 31, 1952. After that date the registration fee will be increased to $30.00 for Regular Members and $15.00 for Associate Members. These fees include tickets for the social events.

Members of the Congress may make their travel arrangements through any agent of Thomas Cook and Sons, which has been selected as the official agency by the Congress, or any travel agency of their choice.

## SEVENTH INTERNATIONAL CONGRESS OF RADIOLOGY, 1953

Arrangements for the forthcoming Seventh International Congress of Radiology to be held in Copenhagen, Denmark, from July 19 to 25, 1953, are well in hand, and it is hoped to circulate the Preliminary Program during the Spring. Copies will be sent to all members of national radiological societies from most of which membership lists have already been received.

It will be greatly appreciated if as many potential members as possible enroll well in advance of the official closing date. This will enable applications to be dealt with more promptly.

The address of the Congress Office is: Seventh International Congress of Radiology, Øster Volgade 10, Copenhagen K, Denmark.

Flemming Nørgaard
*Secretary-General*

## TECHNICAL EXHIBITION SEVENTH INTERNATIONAL CONGRESS OF RADIOLOGY, 1953

An International Exhibition of Roentgenologic Equipment and Accessories is being arranged in conjunction with the forthcoming Seventh International Congress of Radiology and will take place in Forum Exhibition Hall, Copenhagen, Denmark, from July 20 to 24, 1953. A large number of firms have been circularized about the Exhibition and invited to make provisional applications for space. Any firms not having received information about the Exhibition and requiring further details should apply to the Technical Exhibition Committee, Seventh International Congress of Radiology, Øster Volgade 10, Copenhagen K, Denmark.

Dr. E. de Fine Licht, Chairman
*Technical Exhibition Committee*

## OHIO STATE RADIOLOGICAL SOCIETY

The annual meeting of the Ohio State Radiological Society will be held May 24

and 25, 1952, in Mansfield, Ohio, at the Mansfield-Leland Hotel. This is not being held in conjunction with the meeting of the Ohio State Medical Association.

### OKLAHOMA STATE RADIOLOGICAL SOCIETY

The Oklahoma State Radiological Society held its annual combined meeting with the Oklahoma State Association of Pathologists on Sunday, February 3, 1952, at the University Hospital in Oklahoma City. Dr. Peter E. Russo, President of the Oklahoma State Radiological Society, presided.

# BOOK REVIEWS

*Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.*

Post-Graduate Lectures on Orthopedic Diagnosis and Indications. By Arthur Steindler, M.D., F.A.C.S., Professor of Orthopedic Surgery, State University of Iowa, Iowa City, Iowa. Volume I. Section A: Propedeutics in Orthopedic Diagnosis. Section B: Congenital Deformities and Disabilities. Cloth. Price, $7.50. Pp. 289, with 290 illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1950.

The volume described is the first of a projected series of four. It consists of lectures as delivered by the author to his post-graduate students of orthopedic surgery. The completed series is proposed as a guide in orienting the student to the boundary which separates normal and pathological conditions of the locomotor system and, after recognition, the indications for the proper disposition of the pathological conditions.

The first volume of the lectures is divided into two parts: Propedeutics in Orthopedic Diagnosis and Congenital Deformities and Disabilities. The former is divided into four lectures. An analysis of the present knowledge of normal anatomy and physiology of the locomotor system is presented. The second part is divided into seven lectures. The pathogenetic theories, the role of heredity, the chondrodystrophies and related conditions due to defective mesoderm, congenital deformities of the spine and thorax, talipes, anomalous conditions of the lower extremities, congenital dislocation of the hip, and congenital deformities of the upper extremity are discussed. The historical, pathologic and clinical phases of each entity are presented in an orderly logical manner to lead to the indications for management.

Steindler, in inimitable fashion, presents a didactic outline in which he assumes the responsibility for all opinions as in classroom teaching. The student is presented with material from the basic sciences as it is related to the clinical situation being discussed. The indications for accepted treatment are clearly presented. The volume is adequately illustrated. It contains a stimulating bibliography. Case histories are strategically used to clarify points the author chooses to emphasize. The format is very pleasing. The size of the book, a welcome innovation in medical publications, will allow it to be used in comfort.

A master clinician and teacher here presents his organized material to the post-graduate student. A need for such a presentation has long been recognized. All students of orthopedic surgery will profit by such a presentation.

Frank P. Walsh, M.D.

Post-Graduate Lectures on Orthopedic Diagnosis and Indications. By Arthur Steindler, M.D., F.A.C.S., Professor of Orthopedic Surgery, State University of Iowa, Iowa City, Iowa. Volume II. Section A: Paralytic Disabilities. Section B: Static Disabilities. Cloth. Price, $6.00. Pp. 198, with 140 illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1951.

The volume described is the second of a series of four. It consists of lectures as delivered by the author to his post-graduate students of orthopedic surgery. It copies the format and methods of presentation used in the first volume.

This section of the series is divided into two parts. The first consists of six lectures devoted to paralytic disabilities. Poliomyelitis is very adequately discussed as to its pathogenesis, pathology, clinical states, residual problems and their disposition. Paralytic scoliosis and the cerebral birth palsies are discussed separately. The second section consists of four lectures. The lumbosacral syndrome, idiopathic scoliosis, internal derangements of the knee and static deformities of the foot and ankle are examined in an orderly manner.

This volume, it is believed by this reviewer, reflects more than its predecessor the author's own views of the problems presented. Other teachers might select from their experience and the literature a collection of factual material that would justify a different approach toward some disabilities discussed. However, it is Steindler's didactic approach which makes this

series of lectures attractive to the post-graduate student. He does not deviate from pointing out or presenting a clear-cut and logically reached conclusion. The volume is very adequately illustrated. The size, type and paper used pleasantly duplicate the first volume.

A master clinician and teacher presents the second section of his organized material to the post-graduate student. The publishing of the last two sections of the series is anticipated with pleasure.

Frank P. Walsh, M.D.

Handbook of Pediatric Medical Emergencies. By Adolph G. DeSanctis, M.D., Professor of Pediatrics and Chairman of the Department of Pediatrics, Post-Graduate Medical School, New York University-Bellevue Medical Center; etc.; and Charles Varga, M.D., Instructor in Pediatrics, Post-Graduate Medical School, New York University-Bellevue Medical Center; etc. Cloth. Price, $5.00. Pp. 284, with 51 illustrations. C. V. Mosby Company, 3207 Washington Boulevard, St. Louis 3, Missouri, 1951.

As stated in the preface, this is not intended as a textbook of pediatrics but as a guide to pediatric conditions calling for rapid emergency therapy. Although intended primarily as a therapeutic treatise, a basic review of some important signs and symptoms is included in certain conditions to facilitate early treatment. The first five chapters discuss treatment in cardiovascular, gastrointestinal, genitourinary, neurological, and respiratory emergencies, respectively. Next the therapy of drowning and poisoning is considered. The final chapters describe the care of the premature infant, miscellaneous emergencies, and pediatric procedures.

This book should be a valuable reference to those dealing with pediatric emergencies.

Rolfe M. Harvey, M.D.

Confrontations-Radio-Anatomo-Cliniques. Published under the direction of M. Chiray, R. A. Gutmann, and J. Sénèque. Volume IV. Paper. Price, 1250 fr. Pp. 65, with 127 illustrations. G. Doin & Cie.; Masson & Cie., 120, boulevard Saint-Germain, Paris 6e, France, 1951.

Once again we have before us for review one of these valuable collections of interesting proved cases, concise but well presented from the roentgenologic, anatomic and clinical standpoints, and with adequate illustrations, both roentgenologic and photographic. The cases have been well selected and cover well the field of roentgenologic abdominal diagnosis. There are four cases of phrenic hernia, eight gastroduodenal ulcers, four benign tumors of the stomach, several cases of esophagogastrostomy, four cases of gastric neoplasm, several jejunocolic fistulas, a case of phytobezoar, several very interesting duodenal and biliary lesions, a case of internal hernia, and several lesions of the pancreas and colon. The collection terminates with two extremely interesting lesions of the urinary tract. Readers of French would surely enjoy studying this collection of intriguing cases.

James T. Case, M.D.

Chest X-Ray Diagnosis. By Max Ritvo, M.D., Assistant Professor of Radiology, Harvard Medical School; Instructor in Radiology, Tufts Medical School; etc. Cloth. Price, $15.00. Pp. 558, with 418 illustrations and 1 colored plate. Lea & Febiger, Washington Square, Philadelphia 6, Pennsylvania, 1951.

In this book, the author has portrayed illustrations of most of the diseases that one is likely to encounter. The book is not an atlas and cannot be regarded as a text. It will, however, serve a useful purpose as a reference for good ideas in arriving at an analysis of chest roentgenograms.

The author, in the text, follows a modern trend in not using a bibliography. When authors are quoted in the text, no reference of a bibliography is used.

The reviewer was disappointed to observe the lack of emphasis on several things, a few of which may be recorded as follows:

1. The limitations of the roentgenogram as a recording medium of chest lesions is not emphasized. In this text, the reader gets the impression that if there is a lesion within the chest, it will be recorded on the roentgenogram.

2. The limitations of the interpreter are not emphasized. It is well known by experienced radiologists that a relatively large number of lesions will not be seen, even though such lesions are present on the roentgenogram.

3. Roentgenoscopy, although repeatedly mentioned, is not sufficiently emphasized. Roentgenoscopy provides an opportunity to study lung physiology and pathologic physiol-

ogy. Because of the ease with which one can obtain roentgenograms, roentgenoscopy is becoming almost a "lost art" to the modern radiologist. There are a number of tricks in doing roentgenoscopy, which, if done, will provide most useful information. In certain instances, a correct diagnosis cannot be made without adequate roentgenoscopy.

The publishers have presented the material in an attractive manner. The printing is easy to read, the composition of the material on each page is attractive and the illustrations are, for the most part, excellent. It should be stated that the arrows used in certain illustrations are so bold, one would not be impressed with the lesion even if it could be seen.

The reviewer feels that this text is a contribution to and will find a useful place in radiology.

Eugene P. Pendergrass, M.D.

Oral and Facial Cancer. By Bernard G. Sarnat, M.D., F.A.C.S., Professor and Head of the Department of Oral and Maxillofacial Surgery, College of Dentistry, etc.; and Isaac Schour, D.D.S., Ph.D., Sc.D., Coordinator of Cancer Instruction, Professor and Head of the Department of Histology and Associate Dean in Charge of Postgraduate Studies, University of Illinois College of Dentistry, Chicago. With a Foreword by Andrew C. Ivy, Ph.D., M.D., D.Sc., Vice-President in Charge of Chicago Professional Colleges, University of Illinois, etc. Cloth. Price, $6.00. Pp. 300, with 118 illustrations and 2 color plates. Year Book Publishers, Inc., 200 East Illinois Street, Chicago 11, Illinois, 1950.

This short text presents the pertinent facts on oral and facial cancer in an elementary fashion and evidently has been written primarily for the teaching of dental students. Emphasis is placed on the important role of the dentist in the early recognition of intraoral neoplastic diseases and the assistance which he can give the surgeon and radiotherapist in their management. The salient features making for early recognition and diagnosis are clearly and well presented. The problems associated with treatment intentionally are not considered in detail. Nevertheless the discussion is at a superficial level, more so for radiotherapy than surgery. Both receive less attention than surgical and prosthetic reconstructive procedures.

Isadore Lampe, M.D.

Malignant Disease of the Female Genital Tract. By Stanley Way, M.R.C.O.G., Gynaecologist to the Newcastle Regional Cancer Organization; Associate Surgeon, Gynaecological Department, Royal Victoria Infirmary, Newcastle-on-Tyne; etc. Cloth. Price, $5.00. Pp. 279, with 38 illustrations. The Blakiston Company, 1012 Walnut Street, Philadelphia, 5, Pennsylvania, 1951.

This is a book which should have a strong appeal to the radiologist and radiotherapist for it presents, from a very broad and comprehensive viewpoint, the fundamental aspects of cancer of the female genital tract. The author writes as a physician of great experience and sound judgment and, as both qualities are deterrents to dogmatic opinion, no effort is made to advance a thesis for the exclusive use of any treatment technique. The author knows full well the limitations imposed by the nature of the disease on both the surgical and radiotherapeutic methods. The book presents only the author's own wide experience with this kind of cancer and a review of standard authors. The writing, as one has learned to expect in English texts, is excellent. The book, on the other hand, contains nothing new, but it does assemble general information all in one place. The sections on history, diagnosis and pathology are brief but ample in a general review of this kind. The radiotherapeutic problem is very aptly stated for all the various kinds of cancer of the female genital tract. The volume contains no descriptions of either surgical or radiotherapeutic techniques and so, in short, it is a relatively simple but very good presentation of the present state of our knowledge of the treatment of these types of cancer.

J. Robert Andrews, M.D.

Radiologia Austriaca. Herausgegeben von der Österreichischen Röntgen-Gesellschaft. Band III. Cardboard. Pp. 202, with 70 illustrations. Urban & Schwarzenberg, Wien, IX/71, Frankgasse 4 (Schliessfach 4), 1950.

This volume contains thirteen papers, some of monograph dimensions, by fifteen authors. Most of the contributors are faculty members of the University of Vienna or the University of

Innsbruck. One of the contributing authors is a resident of Chile and one of Greece.

Five articles deal with radiotherapy and radiobiology and eight with roentgen diagnostic problems. The papers closely parallel contemporary American radiological thinking. Very little controversial material can be found in them.

Hilde Maier and Roland Maly report their experiments in which spores of *Polypodium aureum* were exposed to gamma rays under selective exclusion of the ultraviolet radiation generated by the fluorescence of surrounding water. The lethal gamma roentgen dose was found to be higher if the ultraviolet radiation was eliminated. Of interest are histological studies of the rat spleen by Rudolf Pape and N. Jellinek, made one-half, three and six hours after irradiation with 2, 5, 30, 50 and 300 r, and one to ninety days after exposure to 200 to 1,000 r given as local or total body treatment or combination thereof. The authors conclude that there is a definite difference in the spleen response to local as compared to general irradiation. Prior irradiation of the spleen with small doses causes acceleration of its regeneration to such an extent that large subsequent depressing doses cannot completely counteract this acceleration. Rudolph Hofstätter presents two uterosalpingograms on which extravasation of iodized oil from the uterus into the infraperitoneal space is shown in addition to normal intraperitoneal oil distribution. Ludwig Psenner shows varying degrees of undermining of the anterior clinoids, depression of the tuberculum sellae and widening of the optic foramina in normal subjects and in proved cases of neurinoma and glioma of the optic nerve, meningioma of the sphenoid and optochiasmal arachnoiditis.

Most of the remaining papers are not based on original work or case material but merely contain well informed discussions of radiological topics. Some of these are of refresher course quality, particularly a differential diagnostic table by A. Ravelli on finely mottled and striated roentgenographic lung densities, which lists (with subdivisions) ninety-three conditions or diseases. This might be of benefit also to the occasional American reader, particularly to teachers of radiology or chest diseases, but requires adequate knowledge of German for its full use.

The paper quality and the half tone reproductions are good, and are considerably better than they were in the previous volumes.

Gerhart S. Schwarz, M.D.

A Manual of Artificial Radioisotope Therapy. Edited by Paul F. Hahn, Cancer Research Laboratories, Meharry Medical College, Nashville, Tennessee. Cloth. Price, $6.80. Pp. 310, with numerous illustrations. Academic Press Inc., Publishers, 125 East 23rd Street, New York 10, New York, 1951.

This book is written primarily as an introduction to the practical therapeutic use of radioactive isotopes. It is an effort to bridge the gap between the research phases of isotope study and the more conventional approaches to radiation therapy.

Each of the fourteen chapters is written by an authority familiar with radioisotopes. The therapeutic problems that are amenable to management by radioisotopes are defined, and criteria for the selection and use of suitable isotopes are established. Timely comments on dosimetry, radiation hazards, and radiation protection are included. The use of radiophosphorus, radioiodine and radiogold are thoroughly reviewed and the status of colloidal radioactive gold for interstitial and intravenous use is discussed.

Chapters on radiological instruments, health physics and procurement of isotopes are presented in orderly fashion and the manual concludes with a practical and useful chapter on "Planning the Radioisotope Program in the Hospital."

The reader is provided with many and diverse expert opinions on isotope problems. The book goes into enough detail to clearly outline the field, but yet is brief enough not to become too complex. The reader is properly left with the thought that, as yet, the field of medical isotopes presents many unanswered questions upon which the inexperienced should proceed with caution. Those inexperienced in the isotope field may feel that the clinical presentations are not brought to a forceful conclusion, but, of necessity, any formulation of strict therapeutic policy in such a rapidly developing field is impossible.

In summary, this manual serves as an introduction to the medical use of radioisotopes in its broader aspects. It is a compact and reliable source for surveying the field.

Hymer L. Friedell, M.D.

## BOOKS RECEIVED

Micro-arteriography. And Other Radiological Techniques Employed in Biological Research. By Alfred E. Barclay, O.B.E., M.D., D.Sc. (Hon.) Oxon., D.Sc. (Hon.) Manchester, F.R.C.P., F.F.R., F.A.C.R., Honorary Radiologist to the Nuffield Institute for Medical Research, Oxford. Cloth. Price, $6.75. Pp. 102, with 46 illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1951.

Über die röntgenologischen Darstellungsmöglichkeiten des weiblichen Genitalapparates mit Hilfe von Jodöl und Jodsol. Von Dozent Dr. med. habil. J. Erbslöh, Bad Oldesloe. Paper. Price, DM 16.80. Pp. 74, with 64 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany, 1951.

Angiocardiography. Annals of Roentgenology. Volume XX. By Charles T. Dotter, M.D., Assistant Professor of Radiology, Cornell University Medical College; Assistant Attending Radiologist, The New York Hospital; and Israel Steinberg, M.D., Assistant Clinical Professor of Radiology and Medicine, Cornell University Medical College; Assistant Attending Radiologist and Physician to Out-Patients, The New York Hospital; etc. Cloth. Price, $16.00. Pp. 304, with 252 illustrations. Paul B. Hoeber, Inc., 49 East 33rd Street, New York 16, New York, 1951.

Clinique et physiopathologie des cardiopathies congénitales opérables. Acta chirurgica Belgica, Supplement I. Rapport au Congrès annuel de l'Association Belge de Chirurgie le 9 juin 1951 à Bruxelles. Par J. Lequime, Université de Bruxelles, et R. Charlier, Université de Liège. Publiés sous la Direction de A. Dumont. Paper. Pp. 115, with 37 illustrations. Acta Medica Belgica, 64, rue de la Concorde, Bruxelles, Belgium, 1951.

Atlas of Tumor Pathology. Section VIII—Fascicle 29. Tumors of the Adrenal. By Howard T. Karsner, M.D., Medical Research Advisor, Bureau of Medicine and Surgery, U. S. Navy, formerly Professor of Pathology, Western Reserve University. Published by the Armed Forces Institute of Pathology. Under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C., 1950. Paper. Price, $1.00. Pp. 60, with 47 illustrations. American Registry of Pathology, Armed Forces Institute of Pathology, Washington 25, D. C.

Plastic Surgery of the Nose. Including Reconstruction of War Injuries and of Deformities from Neoplastic, Traumatic, Radiation, Congenital, and Other Causes. By James Barrett Brown, M.D., Professor of Clinical Surgery, Washington University School of Medicine, St. Louis, Mo.; etc.; and Frank McDowell, M.D., Assistant Professor of Clinical Surgery, Washington University School of Medicine, St. Louis, Mo. Cloth. Price, $15.00. Pp. 427, with 379 illustrations including 48 in color. C. V. Mosby Company, 3207 Washington Boulevard, St. Louis 3, Missouri, 1951.

Tumors of the Skin. Benign and Malignant. By Joseph Jordan Eller, B.S., M.D., Director of the Department of Dermatology, New York City Hospital, New York, etc.; and William Douglas Eller, M.D., Assistant in Dermatology and Syphilology, University Hospital, New York-Bellevue Medical Center, etc. Second edition, thoroughly revised and enlarged. Cloth. Price, $15.00. Pp. 697, with 550 illustrations and 3 colored plates. Lea & Febiger, Washington Square, Philadelphia 6, Pennsylvania, 1951.

La malattia sclerodermica. By Guido Bassi. Prefazione del Prof. Giovanni di Guglielmo. Cloth. Pp. 701, with 185 illustrations. Instituto Editoriale Medico, Via Calzolerie 1, Bologna, 1951.

Radiologic Physics. By Charles Weyl and S. Reid Warren, Jr., Moore School of Electrical Engineering, University of Pennsylvania. With a Foreword by Eugene P. Pendergrass, M.D., Director of the Department of Radiology, University of Pennsylvania. Second edition. Cloth. Price, $10.50. Pp. 491, with numerous illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1951.

Effects of External Beta Radiation. National Nuclear Energy Series, Manhattan Project Technical Section. Division IV—Plutonium Project Record, Volume 22 E. Edited by Raymond E. Zirkle, Professor of Radiobiology, Institute of Radiobiology and Biophysics, University of Chicago, etc. First edition. Cloth. Price, $3.25. Pp. 242, with numerous illustrations and tables. McGraw-Hill Book Company, 330 West 42nd Street, New York 18, New York, 1951.

Research and Training Facilities for Radiobiology and for Use of Isotopes in Biology and Medicine in the United States and Canada. By D. Harold Copp, University of California, Berkeley, California; Now Chairman of the Department of Physiology, Faculty of Medicine, University of British Columbia. Paper. Pp. 151. Division of Mathematical and Physical Sciences, National Research Council, 2101 Constitution Avenue, Washington, D. C., 1950.

Berättelse från Styrelsen för Cancerföreningen i Stockholm över Verksamhetsåret 1950, pp. 1–24. Redogörelser för verksamheten å Radiumhemmet, radiopatologiska institutionen och radiofysiska institutionen vid Konung Gustaf

V:S jubileumsklinik i Stockholm under år 1950, pp. 26–35. Index of Papers published at the Radiumhemmet, the Institute of Radiopathology and the Institute of Radiophysics, pp. 36–61. Report of Dec. 31st, 1950, on patients registered at the Radiumhemmet 1921–1950, pp. 63–130. Paper. Pp. 130, with numerous tables. K. L. Beckmans Boktryckeri, Stockholm, Sweden, 1951.

Law of Hospital, Physician, and Patient. By Emanuel Hayt, LL.B., Lecturer in Hospital Administration, Columbia University and University of Minnesota; Counsel, Hospital Association of New York State, and The Greater New York Hospital Association; Lillian R. Hayt, M.A., J.D., of the New York Bar; and August H. Groeschel, A.B., M.D., M.S., Assistant Director, The New York Hospital; Colonel, Medical Corps, U. S. Army Reserve. Second edition, revised and enlarged. Prepared in Collaboration with the American College of Hospital Administrators. Cloth. Pp. 804. Hospital Textbook Company, 99 Wall Street, New York 5, New York, 1952.

The Photography of Patients. Including Discussions of Basic Photographic and Optical Principles. By H. Lou Gibson, F.B.P.A., A.P.S.A., Medical Division, Eastman Kodak Company, Rochester, New York. Cloth. Price, $5.50. Pp. 118, with numerous illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1952.

Vol. 67, No. 4

# ABSTRACTS OF RADIOLOGICAL LITERATURE

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## ROENTGEN DIAGNOSIS

### Abdomen

Walk, L. Villous tumor of the stomach; clinical review and report of two cases. *Arch. Int. Med.*, April, 1951, *87*, 560–569.

There have been only 51 published cases of villous tumor or cauliflower-like papilloma of the stomach. The author adds 2 cases of his own and reviews the literature, analyzing 48 cases.

These tumors occur in patients aged 30–80 years with peak incidences between 41–50 years and 61–70 years. The cases showing malignant histopathological changes vary directly with the size of the tumor, Thirty-three per cent of tumors measuring 1 to 2 cm. are malignant while those 7 cm. or greater in size will show malignant changes in 75 per cent. Most of the malignant changes are in the stalk of the tumor.

The dominant clinical finding is a severe anemia. This is due to chronic blood loss, and tarry stools are frequently observed. Many patients also have vague epigastric pain and discomfort. On roentgenograms, these tumors show filling defects with a characteristic "soap bubble" surface.

Treatment should be resection of the involved stomach rather than simple excision of the tumor mass. The 2 cases presented are illustrated.—*W. H. Smith, M.D.*

Smith, Hugh P., Jr., and Blakemore, William S. Benign polyp of the ampulla of Vater. *Radiology*, April, 1951, *56*, 571–574.

An unusual case of benign polyp of the ampulla of Vater is presented. Cholangiography done on the tenth day after cholecystectomy, with exploration of the duct and insertion of a T-tube, revealed a filling defect at the duodenal end of the common duct. This was interpreted as a gallstone. On repeat cholangiogram eleven days later the same defect was visualized. Surgery revealed a polyp measuring 1 cm. in diameter in the ampulla of Vater.

A brief summary of the literature on tumors of the ampulla of Vater is given. It is emphasized that, while these tumors are relatively rare, they should be considered in surgical and roentgenological diagnosis especially when no stones are found at operation.—*A. W. Sommer, M.D.*

Hudak, Albert. Le transit accéléré du grêle. (The accelerated passage through the small intestine.) *Radiol. clin.*, May, 1951, *20*, 148–154.

The roentgenologic examination of the small intestine is a long and tedious procedure. The author gives a brief review of the many methods used, most of which are rather complicated.

In this preliminary communication, he describes a method of his own which is "simple, economical and instructive." It consists of the administration of an iced meal followed by intravenous injection of prostigmine. Although the accelerating effects of both the cold and the intravenous prostigmine on the passage of barium through the small intestine are well known, according to the author a combination of the two agents has never been used before.

The technique of the method is as follows: the patient is given 1–2 teaspoonfuls of thick gelobarine and 10 minutes later a glass of iced physiologic saline solution. Another 10 minutes later 1 mg. of prostigmine is injected intravenously. The first roentgenogram of the small intestine is made 10 minutes following the prostigmine injection. The barium reaches the ileocecal region within 30 minutes to 2 hours after the injection. The dorsal decubitus is preferred and, as a rule, 4 to 5 roentgenograms are sufficient for the entire examination.

The author has used the method for approximately one year. The iced meal accelerates the passage through the small intestine on a physical basis. The prostigmine, on the other hand, exerts an inhibitory action of the cholinesterase which catalyzes the disintegration of acetylcholine, thereby further increasing the peristalsis of the small intestine.

Several cases are cited in which the method proved particularly useful and the respective roentgenograms are reproduced to illustrate the pertinent findings.—*T. Leucutia, M.D.*

Cherry, James W., and Hill, Rogers Lee. Leiomyoma of the jejunum; a neoplasm imitating the symptoms of duodenal ulcer. *Arch. Surg.*, April, 1951, *62*, 580–585.

Since duodenal ulcer is 240 to 260 times as common as tumor of the small intestine, the former is naturally considered far more seriously as a diagnostic possibility in a search for a cause of melena and abdominal distress.

The authors were able to collect from the literature 8 cases in which a diagnosis of duodenal ulcer had been made because of a combination of abdominal pain, melena, and (in 7 of the cases) roentgen evidence of duodenal ulcer, but in which at subsequent operation or autopsy a leiomyoma of the jejunum was found instead of a duodenal ulcer. They report an additional case with the same story and findings.

A submucosal leiomyoma may bleed from mucosal erosion but oftenest manifests symptoms by intussusception and obstruction. The subserosal variety may achieve such size as to attract attention to the mass; it bleeds after central necrosis and rupture into the lumen of the bowel has produced a pseudodiverticulum. That these jejunal tumors, when symptomatic, often lead to such irritability of the duodenum as to simulate duodenal ulcer roentgenologically is a reason for diagnostic errors which can be avoided only by constant suspicion and careful roentgen study of the small bowel.—*George Cooper, Jr., M.D.*

Chapple, C. F. Appendiceal calculi; a report of two cases and a brief review of the literature. *Brit. J. Surg.*, April, 1951, *38*, 503–506.

True calculi of the appendix are uncommon. Bunch and Adcock gave the figure as 1 case in 2,000 cases of appendicitis. According to Felson and Bernard, slightly over 100 cases have been reported.

Stones may be small, multiple, and faceted, or large, single, and laminated. Very few authors have made a correct preoperative diagnosis, and differentiation was from renal or ureteral calculi, and gallstones in the gallbladder or impacted in the lower ileum. Differentiation from calcified ileocecal lymph nodes is not usually difficult.

Felson has carried out an investigation on the actual incidence of calculi in diseased and normal appendices. He found that in 75 acutely inflamed appendices 33.3 per cent showed radiopaque material. In 183 normal appendices only 2.7 per cent showed calculi. The relationship of such calculi to appendicitis must be considered. Appendiceal calculi can be placed among the numerous foreign bodies found in the appendix, which include dental fillings, toothbrush bristle, grape seeds, lead shot, etc. It is now agreed that they play some part in the course of acute appendicitis and may lead to earlier perforation once inflammation has commenced.

Two cases of large appendiceal calculus are reported. In each case acute appendicitis with perforation occurred, one with formation of a local abscess and the other with general peritonitis.—*W. C. MacCarty, Jr., M.D.*

Pool, R. M., and Dunavant, W. David. Volvulus of the sigmoid colon. *Ann. Surg.*, May, 1951, *133*, 719–725.

In a study made at the John Gaston Hospital of the University of Tennessee Medical School in Memphis, 48 obstructions of the colon were noted in 522 cases of intestinal obstruction. Sixteen of the 48 cases comprised one-third of the total number of colon obstructions and were definite volvulus of the sigmoid colon. The greatest incidence was between the ages of fifty-one and seventy. The etiological, pathological, diagnostic, and therapeutic problems. of volvulus of the sigmoid colon, as well as the mortality, are briefly discussed. In only 1 case was a barium enema made following a preliminary film of the abdomen.—*Moris Horwitz, M.D.*

McCormick, Norman A. The diagnosis of early cancer of the large bowel and rectum. *Canad. M. A. J.*, May, 1951, *64*, 403–409.

The author relates his experience in dealing with 277 patients who had cancer of the large bowel and rectum. This group out-numbered other groups, such as breast malignancy, female genital cancer, gastric cancer and malignancy of thoracic viscera among 3,605 patients seen during the past fourteen years. Salient points in his experience include:

1. Large bowel malignancy accounts for 15 per cent of cancer deaths in Ontario.
2. Seventy per cent have lesions accessible by sigmoidoscopy.
3. Seventy-two per cent of patients with cancer of the rectum were operable with a mortality of 3 per cent.
4. Fifty-two per cent lived five years or more.
5. A small but definite number of patients with carcinoma of the rectum may be successfully treated with radiation therapy.
6. A sigmoidoscopic examination should be a prerequisite to roentgen examination for cancer of the colon. The author believes that the radiologists in Windsor are justified in reporting, "that their examination does not preclude the possibility of a cancer being present in the rectum."
7. Roentgen investigation does not play the most important role in diagnosis of cancer of the rectum but is of great value in the search for multiple lesions of the colon in the presence of rectal malignancy.—*J. W. Turner, M.D.*

Jones, Henry H., Kaplan, Henry S., and Windholz, Frank. Air-contrast colon examination with colloidal barium. *Radiology*, April, 1951, *56*, 561–566.

A method of doing the double contrast examination of the colon is described. One of the authors developed a colloidal suspension of barium sulfate (details not included in this article) which has been found to coat the colon mucosa satisfactorily.

Castor oil preparation is advocated and where good results are not obtained cleansing saline enemas are given. The special colloidal suspension of barium is very thick and pressure is required to force it into the colon. After the colon has been filled to about the splenic flexure the air is then introduced. Turning the patient aids in distributing the barium and air. The standard roentgenographic positions employed are erect posteroanterior, left and right lateral decubitus and posteroanterior Trendelenburg.

The authors state that any questionable polypoid lesion must be checked by subsequent examination.—*C. A. Stevenson, M.D.*

Mayo, Henry W., Jr., and McKee, Edward E. Carcinoid of the rectum. *Arch. Surg.*, April, 1951, *62*, 506–513.

Carcinoids of the gastrointestinal tract are most frequently found in the appendix. The rectum is one of the least common locations. There are 66 known cases of carcinoid of the rectum reported to date. The authors have reviewed the clinical data on the known cases and have presented 2 additional cases. The histopathologic picture is briefly reviewed. Since

previous reports have dealt largely with the histologic and pathologic features, the present review emphasizes the clinical characteristics.

Carcinoids arise from the submucosa and invade the adjacent mucosa and muscularis. The consensus is that all are malignant although they grow slowly. Metastases occur late in the course of the disease. Removal of the primary lesion frequently results in symptom-free intervals of many years, even in the presence of known metastases.

The age of the patients varied from fourteen to seventy-one years. The majority of cases had no symptoms referable to the local lesion. Symptoms, when recorded, usually included bloody stools and occasionally constipation, tenesmus and lower abdominal pain. Most of the lesions were less than 1 cm. in diameter and were located in the lower part of the rectum covered with mucosa.

Many lesions were sessile, a few pedunculated and polypoid. In only 3 cases were lesions multiple. Metastases were recognized in 9.1 per cent of cases. Local excision has been the usual surgical procedure Larger lesions producing constriction or annular defects required abdominoperineal resection.

No mention has been made of roentgen diagnosis, most lesions having been discovered by means of proctologic examination.—*C. N. Borman, M.D.*

Gottlieb, Charles, Dorfman, Milton, and Cregg, Hugh A. Pancreatitis: its preoperative diagnosis by gastro-intestinal roentgenography. *Radiology*, April, 1951, *56*, 528–534.

The opacified duodenum may present some roentgen signs suggestive of pancreatic disease. Frostberg first called attention to the inverted "3" sign as caused by enlargement of the head of the pancreas with subsequent deformity of the descending duodenum. Since that time many authors have described changes in the duodenum and stomach secondary to enlargement of the pancreas.

The following roentgenologic signs are considered suggestive of pancreatic enlargement: (1) inability to fill a segment of the descending duodenum, (2) narrowing of the descending duodenum, (3) dilatation of the duodenum above an area of narrowing, (4) coarsening or effacement of the duodenal folds on the pancreatic side. (5) flattening of the valvulae conniventes, (6) extrinsic pressure deformity of the duodenal bulb or pyloric portion of the stomach, (7) widening of the duodenal curve, (8) abnormal duodenal retention of barium, (9) deficiency pattern in the small bowel, (10) localized ileus.

Nine cases are reported in which the roentgenologic findings were of aid in the diagnosis of pancreatitis but the authors state that these findings are also present in malignant disease of the pancreas. The common denominator in all 9 cases was encroachment of the enlarged pancreas on the duodenum.

Differential diagnosis of pancreatic enlargement and primary tumors of the duodenum is important. The normal ampulla of Vater may appear as a small extramucosal tumor and aberrant pancreatic tissue may produce single or multiple nodules without extrinsic pressure on the duodenum. Other extrinsic pressure usually is not on the pancreatic side.—*C. A. Stevenson, M.D.*

Mikal, Stanley, and Campbell, Alexander J. A. Carcinoma of the pancreas; diagnostic and operative criteria based on one hundred consecutive autopsies. *Surgery*, Dec., 1950, *28*, 963–969.

One hundred cases of carcinoma of the pancreas and 8 cases of carcinoma of the papilla of Vater were analyzed at necropsy. Two-thirds of the carcinomas occurred in the head of the pancreas and one-third in the body and tail of the pancreas. The disease was noted predominantly among males in a ratio of 2:1, and more than 90 per cent of the patients were past the fifth decade of life. The majority of pancreatic carcinomas were found to be duct cell adenocarcinomas, although squamous cell, colloid and papillary cystadenocarcinomas also occurred. In this series, gross pancreatitis with fat necrosis was present in 23 per cent of the patients with pancreatic carcinoma; 2 patients had intrapancreatic lithiasis. Pancreatic cysts were present in 15 per cent of the patients. Stones comprised part of the contents of 1 cyst.

Cholecystitis was found in 42 per cent of the patients, and cholelithiasis was found in 20 per cent. The gallbladders of 74.6 per cent of the patients with carcinoma of the head of the pancreas and of 17.9 per cent of those with carcinoma of the body and tail were dilated. Six of the 8 patients with vaterian carcinoma had dilated gallbladders. The common bile duct was found to be a more accurate indicator of an existing pancreatic carcinoma than a dilated gallbladder. The common bile ducts of 86.6 per cent of the patients with carcinoma of the head of the pancreas and of 14.8 per cent of those with carcinoma of the body and tail were dilated. Dilatation of the gallbladder or common duct among patients with carcinoma of the body and tail of the pancreas was usually due to carcinomatous invasion of the common bile duct or metastatic lymph node compression of the common bile duct.

Eighty-eight per cent of the patients with carcinoma of the head of the pancreas, 27 per cent of the patients with carcinoma of the body and tail, and 87 per cent of those with carcinoma of the papilla of Vater were jaundiced. Thrombophlebitis occurred among 18 per cent of patients with carcinoma of the head of the pancreas and 48.5 per cent of those with carcinoma of the body and tail. Diabetes mellitus was an associated finding among 13 per cent of the patients.

Gastroduodenal ulcerations from neoplastic in-

vasion, simulating a bleeding peptic ulcer, occurred among 20 per cent of the patients with carcinoma of the pancreas. Of these ulcerations, 18 were in the duodenum and 2 were in the stomach. Three of the 8 patients with carcinoma of the papilla of Vater were found to have duodenal ulcerations. Of the patients with duodenal ulceration, 3 had massive hemorrhage.—*P. G. Dillard, M.D.*

Herrmann, K. O. Die Entleerung der menschlichen Gallenblase im Röntgenserienbild; eine röntgenphysikalische Darstellung. (The emptying of the human gallbladder in serial roentgenograms; a roentgenological physical demonstration.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, April, 1951, *74*, 421–424.

An attempt has been made to study the physiology of evacuation of the bile by the bile ducts in 2 patients with cholecystostomy.

Contrast medium was injected without pressure with the purpose of duplicating the normal physiology as much as possible.

It was shown that the common duct fills and empties in three separate and independent segments. The filling can occur from the cystic duct, but is not necessarily dependent on the condition of either cystic duct or gallbladder.

The sphincter of Oddi represents a very sensitive muscle the purpose of which does not lie in the closure of the common duct, but rather indicates active participation in the emptying process of the bile system.—*H. P. Mueller, M.D.*

Dunne, Edward F., Jensen, Esther H., and Hughes, C. Robert. Preliminary study of a new cholecystographic medium. *Cleveland Clin. Quart.*, April, 1951, *18*, 98–101.

The authors studied the side effects and concentration or intensity of visualization of the gallbladder shadow in 232 unselected patients, half of whom received priodax and half telepaque. The latter is the new organic compound, 3-(3-amino-2,4,6-triiodophenyl)-2-ethyl-propanoic acid, which contains 66.68 per cent iodine by weight, in organic combination compared with 51.38 per cent in priodax. Nine tablets (4.5 gm.) of priodax and 6 tablets (3 gm.) telepaque were employed for the respective patients of each group.

Side effects consisting of mild and severe nausea, vomiting, mild and severe diarrhea and dysuria were reported in 60 per cent of the priodax group and in 21.4 per cent of the telepaque series. Diarrhea occurred in 42.1 per cent of the priodax series as compared to 12.0 per cent in those receiving telepaque.

Excellent concentration of the dye was noted in 40 per cent of the telepaque group and 20.5 per cent in the priodax series. While this difference is not statistically significant in this study it suggested the possibility that smaller doses of telepaque may be sufficient for satisfactory visualization. A second series of patients are being studied with a dosage of 2 gm. of telepaque.—*J. N. Ané, M.D.*

Packard, George B., and Reynolds, Levi E. Meconium peritonitis. *Ann. Surg.*, April, 1951, *133*, 548–554.

Meconium peritonitis is an entity which has been recognized since 1838. Over 100 cases have been reported to date. Meconium reaches the ileocecal junction by the fourth month and the rectum by the fifth. Anything blocking the onward passage of the meconium results in bowel distention, perforation occurring if this is pronounced enough. Fetal meconium peritonitis is usually due to an obstruction caused by stenosis, atresia, volvulus or bands, but is occasionally produced by a defective blood supply. In the fetus the meconium is sterile and some perforations heal, leaving a partially calcified plaque. The meconium becomes contaminated by bacteria by about the third day of extrauterine life and postpartum meconium peritonitis is, as a rule, fatal. It occurs at or immediately after birth. Obstruction is thought to be the etiological factor in about 50 per cent of the cases. This is usually due to stenosis, atresia or constricting bands, but in some cases to volvulus and hernia. Occasionally meconium ileus is a factor, the tenacious putty-like material blocking the intestine; this unusual consistency is, as a rule, associated with interstitial pancreatitis and fibrosis. Trauma is believed to be a determining factor in about 50 per cent of the cases, both intra- and postpartum.

In cases of intrapartum peritonitis the chief sign is distention which may be present immediately at birth, the infant being in distress, the color being poor and the respiration grunting. Vomiting occurs soon after birth and soon becomes bile stained. No bowel movements occur as a rule. The symptoms are progressive until death one to four days after birth. Roentgenograms of the abdomen reveal dilated loops of small bowel; occasionally calcified plaques are noted indicating previous fetal peritonitis. Of most importance is the presence of free air in the abdomen.

The writer describes 2 cases. The first case was that of a baby boy twenty-nine hours old with a swollen abdomen and history of emesis of bile. There had been no bowel movements and no meconium. Respirations were shallow and there was cyanosis. The roentgenograms revealed a large area resembling a cyst in the abdomen, containing fluid and air with no gas in the colon or rectum, there being dilated loops of small intestine. A cyst or diverticulum communicating with the bowel was considered. Surgery revealed this large cavity containing bowel contents and gas with the intestines matted together by ad-

hesions. A communication was noted with the small intestines. The child died five hours after surgery. The pathologic diagnosis made at autopsy was meconium peritonitis, congenital malrotation of the intestinal tract, congenital volvulus with rupture of the intestinal tract with secondary pulmonary findings. It is probable that the volvulus occurred during intrauterine life and was secondary to malrotation which produced intestinal obstruction and then rupture of the ileum with the consequent meconium peritonitis.

The second case was that of a child forty-eight hours old. Labor had been difficult, followed by a frank breech delivery. Soon after birth the child vomited, the emesis being green. The abdomen was distended, there being a progressive increase of this distention. Roentgenograms revealed a large quantity of free air in the abdomen and a diagnosis of a ruptured hollow viscus was made. Surgery revealed much greenish fluid in the peritoneal cavity with lumps of meconium. The fluid was removed by aspiration. The loops of intestines were found matted together and adherent, being covered with fibrin; considerable distention was present. Inspection did not reveal the opening, which evidently was sealed over. Drainage was instituted. The child later developed a fecal fistula but ultimately made practically a complete recovery. In this case it is probable that the perforation occurred as a result of birth trauma. The early recognition and adequate treatment of the peritonitis before secondary infection resulted in a successful outcome.—*J. P. Bennett, M.D.*

## Gynecology and Obstetrics

Pack, George T., and Scharnacel, Isabel M. The prognosis for malignant melanoma in the pregnant woman. *Cancer*, March, 1951, *4*, 324–334.

The stimulating effects of hormones on benign nevi and malignant melanoma have long been recognized. Occasionally the transformation of a benign nevus into a malignant melanoma occurs during pregnancy, and such tumors grow wildly and disseminate very rapidly. In 1,050 cases of melanoma, 32 were associated with pregnancy; 14 of these were dead of tumor in three years, 2 have survived eight years, and the remainder were treated too recently for evaluation.

Methods of treatment included radical surgery, irradiation of tumor site and/or pituitary, and hormonal withdrawal, the latter by castration. Only radical surgery offers a slight hope for cure. Therapeutic abortion is not indicated, for it does not influence the course of the disease.—*R. A. Silver, M.D.*

Ingram, James M., Jr., and Novak, Emil. Endometrial carcinoma associated with feminizing ovarian tumors. *Am. J. Obst. & Gynec.*, April, 1951, *61*, 774–789.

The authors briefly review the literature and report on 4 new cases of endometrial carcinoma associated with feminizing ovarian tumors. It is now believed that both thecoma and granulosa cell tumors have their origin in the undifferentiated cells of the ovarian mesenchyme The luteoma is thought to represent the complete or partial luteinization of the thecoma or granulosa cell tumor. Because of their common histogenesis and frequent co-existence, the term feminizing mesenchymoma of the ovary has been suggested by Novak to include all these tumors.

Fifty cases of combined tumors were found in the literature, including 28 thecomas and 22 granulosa cell tumors. Biskine's studies indicate that granulosa cell tumors possess a lower degree of carcinogenic capacity than thecomas presumably the result of lower estrogen production. All the patients were postmenopausal and bleeding was the presenting symptom.

Sixty-six cases of feminizing tumors of the ovary at Johns Hopkins Hospital were reviewed and 4 adenomacarcinomas of the endometrium were found. The case histories in these are presented as well as 1 case of ovarian tumor associated with cancer of the breast. Various investigators have reported that 5–27 per cent of postmenopausal women with feminizing tumors develop endometrial cancer. The findings seem to coincide with Loeb's theory that tissues must remain under influence of estrogens for a prolonged period before they can exert a carcinogenic effect. Hyperplasia accompanies a majority of estrogen-producing tumors. Many of these patients bleed for years before the hyperplasia gives rise to carcinoma. Five of the 66 patients had previous pelvic irradiation.—*Martha E. Mottram, M.D.*

Nelson, Kinloch, and Dennison, Charles W. Pelvic tumors with ascites, hydrothorax, or both (Meigs's syndrome). *Ann. Int. Med.*, April, 1951, *34*, 1055–1062.

In a female patient with a pelvic tumor and with ascites or hydrothorax, or both, a diagnosis of malignant tumor with metastasis is sually made. It is not sufficiently known that benign pelvic growths may also be associated with such accumulations of fluid. Even when the tumor is malignant, the fluid may not represent peritoneal or pleural involvement. The purpose of this report is to call attention to such occurrences.

Of greatest significance is the remarkable recovery of such patients following removal of the tumor when it is benign, and the failure of the fluid to return for months or years, at least in some cases even though the tumor is malignant.

The authors' material, though small, indicates that such findings are infrequent. Thus, of 12 cases of

dermoid, 5 of teratoma, 8 of cystadenoma, 3 of fibroma, 2 of endometrioma, 4 of cystoma and 1 of Brenner's tumor (35 cases in all) there were 2 cystic tumors with twisted pedicles and small amounts of ascitic fluid, and 1 teratoma of the ovary with massive ascites.

The authors report in detail: (1) a patient with an ovarian teratoma, largely composed of thyroid tissue, associated with massive recurrent ascites, in whom the fluid did not re-accumulate and whose health was restored after removal of the tumor; (2) a patient with papillary adenocarcinoma of the ovaries and retroperitoneal lymph nodes, with ascites and hydrothorax, but with normal peritoneum at operation and without roentgen evidence of pleural or pulmonary metastases, in whom the fluid did not re-accumulate for twenty-nine months after removal of the tumors, despite the retroperitoneal mass proved as carcinoma by transperitoneal biopsy.

It appears that fibroids of the uterus and ovarian tumors of many types, both benign and malignant, may develop inexplicable ascites, hydrothorax, or both. In some cases this fluid has been bloody. The basis for its formation remains obscure. In 2 cases Meigs demonstrated that the fluid passed from the abdominal to the pleural cavity. Not only is the cause of its occurrence unknown, but why some cases show little or no ascites but massive hydrothorax is even more difficult to explain.

The authors wish to broaden the term "Meigs's syndrome" to include all cases of pelvic tumor, benign or malignant, solid or cystic, with either ascites or hydrothorax alone, or with both, in which no ostensible explanation, such as metastasis, can be found for these accumulations of fluid. By definition, this fluid should be "cured" by removal of the tumor. In malignant tumors with later spread to the peritoneum the fluid may recur.

Exploratory laparotomy is recommended in all patients showing a pelvic mass and ascites, hydrothorax, or both. The finding of a primary tumor elsewhere, such as in the stomach, would, of course, alter this recommendation.—*S. N. Tager, M.D.*

Leventhal, M. L., and Cohen, M. R. Bilateral polycystic ovaries, the Stein syndrome. *Am. J. Obst. & Gynec.*, May, 1951, *61*, 1034–1046.

The characteristics of this syndrome as reported by Stein and his associates are "menstrual irregularity featuring amenorrhea, a history of sterility, masculine type of hirsutism, and, less consistently, retarded breast development and obesity. The ovaries are similarly and simultaneously enlarged, and show typical cystic changes which are irreversible and refractory to hormonal therapy. The development of this condition is not congenital; neither is it inflammatory nor degerative. It is the result of a definite endocrine disturbance."

The authors discuss the pathogenesis, diagnosis, and pathology of this syndrome. They also analyze 10 cases of bilateral polycystic ovaries with amenorrhea and/or sterility and give 8 case reports.—*C. D. Frey, M.D.*

Javert, Carl T., and Finn, William F. Arrhenoblastoma; incidence of malignancy and the relationship to pregnancy, to sterility, and to treatment. *Cancer*, Jan., 1951, *4*, 60–77.

This article offers statistical and clinical data obtained from a questionnaire sent to various sources concerning proved cases of arrhenoblastoma. Only 121 cases were reported through 1949 including 3 cases observed by the authors.

The etiology is unknown, but the theories advanced are listed in the article. Arrhenoblastoma appears usually as a solid tumor and is confined to one ovary in 95 per cent of the cases.

The tumor manifests itself clinically with the features of masculinization and amenorrhea. It was noted that the incidence of pregnancy prior to the development of the tumor was normal and the opportunities of pregnancy following the surgical removal of the tumor was the same for any individual with a unilateral salpingo-oophorectomy. Consequently, conservative surgical procedures are advocated unless malignant changes are evident. The simultaneous occurrence of pregnancy with the tumor is noted rarely owing to the amenorrhea and virilization. The results of this study indicate a 26 per cent incidence of malignancy in arrhenoblastoma. The reports of other authors have listed the figures of malignancy from 10 to 20 per cent. The criteria favoring the diagnosis of malignancy depend upon the histology, anatomical extent, recurrence, and the presence of metastasis. None of the patients with malignant arrhenoblastoma have been known to survive.

Providing the remainder of the genital tract, namely, the uterus and opposite ovary and tube are normal, it is proposed that a unilateral salpingo-oophorectomy be performed initially since at the time of surgery it is usually evident whether the tumor is benign or malignant. Weight loss, ascites, hydrothorax, rapid growth, invasion, and bilateral involvement of the ovaries are indications of malignancy and total hysterectomy and bilateral salpingo-oophorectomy are mandatory. Of course, the tumor should be subjected to histological study for evaluation. Recurrence is indicated by the return of the signs and symptoms outlined above including a recurrence of virility.

Little is said about the relative merits of radiation therapy in patients with arrhenoblastoma. It is merely stated that surgical treatment is preferred. —*J. W. Wilson, M.D.*

Dockerty, M. B., Lovelady, S. B., and Foust,

G. T., Jr. Carcinoma of the corpus uteri in young women. *Am. J. Obst. & Gynec.*, May, 1951, *61*, 966–981.

The authors report 36 cases of proved carcinoma of the body of the uterus in women under forty years of age. The material was gathered from files of the Mayo Clinic from 1905 through 1944. In the same period of time 1,694 cases of carcinoma of the body were found in patients over forty years of age. The 36 cases under forty comprised 2.1 per cent of the total. Fifteen of the patients were less than thirty-five years of age. The rest were in the thirty-five to thirty-nine year age bracket. Eight of the group were single, and 28 were married. A high incidence of infertility was noted. Symptoms included menometrorrhagia, polymenorrhea, dysmenorrhea, leukorrhea, sterility and infertility, for the most part. Additional symptoms were abdominal tumor, backache, headache, arthritis, weakness, loss of weight, and constipation.

Clinically a large portion of the group was obese. Three of the obese patients exhibited hirsutism. Ten patients had hypertension. Less than 20 per cent showed signs of weakness or pallor.

The authors discuss the treatment and pathologic findings of their cases.—*J. M. Kohl, M.D.*

Hirst, John C. Carcinoma of the cervix uteri during pregnancy, with special reference to comparison of sponge biopsies with diagnostic Papanicolaou smears. *Am. J. Obst. & Gynec.*, April, 1951, *61*, 860–871.

At the Philadelphia General Hospital, the author found 0.75 per cent early cervical cancers in 3,674 pregnant women, of whom 1,632 were screened by cytologic methods.

There were only 150 normal appearing cervices in 446 pregnant women; the others showed erosion, cystic changes or polyps, and at least one-half required cytologic screening to rule out tumor.

Both smear and sponge cytology proved as accurate as in the nonpregnant women. Punch biopsy, but not sharp conization or ring tissue biopsies, are safe in pregnancy. The histologic changes in pregnacy consist mainly of decidual reaction, epidermization and hyperactivity of basal cell layers. When compared with each other, Papanicolaou smears yield more false positive and gelatin sponge biopsies more false negative readings.

The dormant period of cancer in situ probably averages five to six years and in invasive cervical cancer may also be a matter of years. The author recommends conservative handling of cancer in situ during pregnancy with repeated cervical cytologic tests and punch biopsies, followed by postpartum ring biopsy and coagulation or cauterization. He advises radical surgery for early stage cervical cancer in early pregnancy. In late pregnancy cesarean section or cesarean hysterectomy followed by irradiation is indicated.—*Martha E. Mottram, M.D.*

Simon, J. Calcifications placentaires; étude clinique, histologique et radiologique. (Calcifications of the placenta; clinical, histological and roentgenological study.) *Bull. féd. Soc. de gyn. et d'obst.*, 1951, *3*, 408–417.

After a critical review of the literature dealing with the pathogenesis and clinical significance of calcification of the placenta, the author describes the histologic and roentgenographic appearances of two placentas obtained from the same woman during two different pregnancies, showing considerable histologic but less definite roentgenographic differences. An examination of the roentgenograms of 25 calcified placentas disclosed that the calcifications usually are needle shaped and occur predominantly in the periphery of the cotyledons. Roentgenographic differences were due solely to the amount of calcium deposited, although the histologic findings often differed greatly. Thus there was no correlation between roentgenographic and histologic findings, nor could correlations be established between the presence and degree of calcification, on the one hand, and the weight of the placenta, weight and sex of the baby, evolution of gestation, type of delivery, puerperal state, Rh factor, serologic findings and parity of the mother, on the other. Ingestation of calcium during pregnancy did not seem to play a part, although the patient under discussion had received calcium and one massive dose of vitamin D during the fourth month of her first pregnancy, combined with ultraviolet radiation to the whole body. Many pregnant women, however, have taken larger doses of calcium and vitamin D without showing calcifications of the placenta. Among 100 unselected specimens examined histologically, 19 placentas showed appreciable calcification, 28 definite calcification, 20 questionable calcification, and 33 no calcification.

The author concludes that calcifications in the placenta are not as frequent, important or typical as one would expect; that their histologic appearance is not yet clearly established; and that their clinical significance is not yet understood. It is conceivable that these calcifications are physiological and due to the progressive and natural aging of the placenta, their roentgenographic appearance being a matter of degree rather than kind.—*Albert Oppenheimer, M.D.*

Savage, John E. Clinical and roentgen pelvimetry: a correlation. *Am. J. Obst. & Gynec.*, April, 1951, *61*, 809–823.

At the University of Maryland, patients in the dystocia clinic of the Department of Obstetrics are measured clinically and by roentgen pelvimetry.

The author compared the two methods in a group of 200 patients.

The Walton-McLane isometric method of pelvimetry was used. The author considers as normal a pelvis in which the Mengert index is greater than 125 for the inlet and 105 for the midplane. He found that the clinical diagnosis of contracted pelvis is made more often than it is actually present. Thus, of 162 patients referred to the dystocia clinic because of clinically contracted pelvis, only 42.5 per cent were found to actually have contracted pelvis by roentgen pelvimetry. Of 42 patients with inlet contraction, 42.8 per cent had dystocia, and of 37 with midplane contraction, 62.1 per cent had dystocia.

The author had 55.3 per cent operative deliveries in the android type pelvis and 50 per cent in the platypelloid type. The other two types, gynecoid and anthropoid, showed about 42 per cent dystocia. (It must be remembered that this is a selected group with expected dystocia.)

A prolonged labor occurred about as frequently in the contracted as in the normal pelvis. The author emphasizes that other factors beside pelvic size and configuration are involved in the prolongation of labor. Sixteen per cent of the 200 patients had cesarean sections. Premature labor did not occur more frequently in patients with contracted pelvis than in patients with normal pelvis. Abnormal presentations or positions occurred in 13.5 per cent.

Attempts to correlate clinical with roentgen classification of pelves showed that the clinical classification was correct in 62.5 per cent of the patients, the anthropoid being the most frequently misdiagnosed type. Attempts to predict the outcome of labors by pelvic measurements showed a correct prediction in 95 per cent of the cases by the dystocia clinic of the Department of Obstetrics and 88 per cent by the Department of Roentgenology.

The author found that clinical contraction of the transverse ischial diameter of the outlet (less than 8.5 cm.) points to midplane contraction in 1 out of every 3.5 cases and to contraction of the inlet in 1 out of every 3 cases. He further found that in patients with a diagonal conjugate greater than 11.5 cm. an adequate inlet is anticipated but below this, there may be dystocia, and roentgen pelvimetry is indicated.

One of the discussants again questions the safety of the roentgenographic examination, but all the others agree with Savage that roentgen pelvimetry has a definite place in determining pelvic size, shape and possibly dystocia.—*Martha E. Mottram, M.D.*

## Genitourinary System

Byrne, John E., and Melick, William F. Subcutaneous urography; description of a new method utilizing 70% urokon and hyaluronidase (a preliminary report). *Urol. & Cutan. Rev.*, April, 1951, *55*, 193–199.

This paper is a report of the value of 70 per cent urokon with hyaluronidase. The authors have studied 25 infants under twelve months of age by this method, and in 68 per cent of the cases were able to obtain satisfactory pyelograms.

Seventy per cent urokon, when buffered to a pH of 7, produces very little reaction in the subcutaneous tissues or in the muscles. Urokon contains 65.8 *per cent* iodine and has a roentgenographic density approximately that of skiodan.

Preparation for the intravenous study in these infants consisted of a small enema the evening before and the morning of the excretory pyelographic study. Elixir of phenobarbital is given for sedation and a milk feeding is given to the infant as soon as the dye can be visualized in the kidneys. The purpose of this is to distend the stomach with air so that the kidneys can be seen through the radiolucent shadow.

Hydase, 75 cc., is injected subcutaneously on the lateral aspect of each thigh. Immediately following this, urokon 70 per cent, 0.5 gm. per kilo, which has been previously warmed to body temperature, is injected into the area previously prepared with the hyaluronidase. The first film is then exposed in approximately twenty minutes and subsequent exposures are made as indicated by the elaboration of the contrast medium in the urinary tracts. The average appearance time of the medium was forty-five minutes.

There was no evidence of sensitivity to the 70 per cent urokon, and the tissue reactions were minmal.

The usual sensitivity tests for organic iodides were carried out prior to the injection.—*G. W. Chamberlin, M.D.*

Apgar, Virginia, and Papper, E. M. Pheochromocytoma; anesthetic management during surgical treatment. *Arch. Surg.*, May, 1951, *62*, 634–648.

The authors review 91 cases of this condition in which surgical removal has been performed and point out that the total mortality rate has been 24 per cent. The serious and fatal consequences of the disease are associated with an excessive secretion of epinephrine and arterenol. These tumors occur equally in both sexes and the age incidence varies from 1½ months to 68 years. In 90 per cent of the reported cases the lesion was benign.

The benzodioxan, cold pressor and histamine tests are reasonably simple and accurate and should be used in any given patient suspected of suffering from this disease. Demonstration of the tumor in the adrenal region by pyelography or air injections has been moderately sucessful, but tumors located in other areas will usually not be demonstrated by these methods.

Anoxia in any form is the greatest pitfall in anesthetic management for it stimulates secretion of the adrenal medulla. If not avoided, uncontrollable tachycardia and hypertension, usually followed by circula-

tory collapse, are apt to occur. The patients tolerate postural changes poorly so that anesthesia should be induced and maintained in the position of the operation. The tumor should be removed with a minimum of manipulation to avoid flooding with epinephrine and arterenol. A preliminary intravenous drip is mandatory. Premedication should not be heavy but otherwise is not of direct importance. Spinal anesthesia should be avoided. Tranquil induction with thiopental sodium followed by maintenance with ether through an endotracheal airway is a safe method of anesthesia which satisfies most requirements.—*A. E. Childe, M.D.*

Günther, G. W. Die Gestalt der oberen Harnwege bei der Sphinkterstarre der Blase. (The condition of the upper urinary tract in rigidity of the sphincter of the bladder.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, April, 1951, *74*, 440–449.

Sclerosis, hypertony or hypertrophy of the sphincter of the bladder is not a rare condition. It occurs in males regardless of age and occasionally in women, produces similar symptoms as prostatic hypertrophy and has been called prostatism without prostate.

It was found that this condition is almost always accompanied by abnormalities of the upper urinary tract, such as abnormal arrangement of the renal pelvis and the calyces, hydronephrosis, double kidney or others.

Distention of the renal pelvis on excretory urograms, hydronephrosis, distention or elongation of the ureters, in cases in which no other causes can be found, should be thought of as significant signs and be considered accordingly, particularly when functional disturbances of the bladder are present.

A valuable roentgenological sign for the diagnosis of an abnormal sphincter of the bladder is a double fluid level in an upright double contrast cystogram. This is caused by the collection of a small amount of dye in a shallow recess which is formed by the hypertrophy of the plica interureterica.—*H. P. Mueller, M.D.*

Kirschbaum, Jack D., and Wilson, Hal T. Calcinosis of the kidneys associated with parathyroid tumor; clinical and pathological study with case report. *Urol. & Cutan. Rev.*, May, 1951, *55*, 264–268.

This is a case report of a sixty-one year old white female, who was admitted to the San Bernardino County Hospital because of a fracture of the left femur. Her past history indicated that she had had bone pains for years and had been treated in the out-patient department of that hospital for hypertrophic arthritis. The roentgen examination showed large cystic lesions in both femurs and a pathological fracture of the left femur just below the trochanter. The films of the skeleton and of the abdomen showed demineralization with multiple cystic bone lesions and with bilateral renal calcification. The laboratory studies showed an anemia with 56 per cent hemoglobin; blood phosphorus was 6 mg. per cent; and the blood calcium was 11 mg. per cent. The patient developed uremia and the nonprotein nitrogen rose to 176 mg. per cent. The blood chlorides were 436 mg. per cent.

At necropsy the important finding was a pedunculated tumor lying in the anterior mediastinum and weighing 37 grams. Histological section of this tumor showed it to be a parathyroid adenoma. Both kidneys showed multiple calculi in the calyces and throughout the renal parenchyma there was a stippling of calcium deposits. The glomeruli were hyalinized and surrounded by fibrous tissue infiltrated with lymphocytes. Calcium deposits were found in the interstitial tissues of the renal parenchyma often surrounding the renal tubules but not within the tubular epithelium or within the lumen of the tubules.

The authors discuss the signs and symptoms of hyperparathyroidism and its sequelae.—*G. W. Chamberlin, M.D.*

Dunn, George P., and Gibson, Thomas E. Extrarenal calyces. *Urol. & Cutan. Rev.*, May, 1951, *55*, 259–263.

The authors report a case of a left pelvic ectopic kidney with developmental defects in the mesenchymal portion of the kidney and a severe degree of extrarenal calyceal development in a twenty-five year old Negro male. A review of the literature shows that 5 other cases of extrarenal calyces have been recorded, all of these associated with defects in the metanephrogenic mass in which there has been a poorly developed renal parenchyma. Some of the cases were associated with ectopic kidneys and with anomalies of position and blood supply. Reproduction of a retrograde pyelogram and photographs of the anatomical specimens of this case and drawings of the previous cases reported are included in this article. They represent excellent illustrations of this anomaly.—*G. W. Chamberlin, M.D.*

Alldred, A. J., and Higgins, T. T. The ectopic ureter in childhood; with an account of four personal cases. *Brit. J. Surg.*, April, 1951, *38*, 460–466.

The ectopic ureter is a rare anomaly. Fraser suggested an approximate incidence of 1:130,000 persons. Only some 300 cases have been recorded. The authors report 4 cases met with in the Urological Service of the Hospital for Sick Children, Great Ormond Street, London.

In the male an ectopic orifice may occur anywhere between the site of the normal ureteric openings and the verumontanum. It may rarely be in the vas deferens or the seminal vesicles. In the female the common sites are in the urethra, the vestibule, and the vagina. Openings have also been reported in the uterus, cervix, and rectum.

The most common symptoms are incontinence or infection, the former being more frequent in females and the latter in males. Incontinence may be absent or "postural." The postural type is remarkable; in spite of the passage of urine at normal intervals the child is constantly wet by day when ambulant, but perfectly dry by night or when lying down. Incontinence of this type is almost pathognomonic of an ectopic ureter.

The diagnosis can be established by an accurate history, careful inspection of the genitalia, cystoscopy, indigo carmine dye studies, and retrograde and excretory urography. The authors emphasize the value of excretory urography when a confirmatory ureterogram by direct catherization of the ectopic ureter cannot be obtained. The pyelograms will serve to outline a double kidney and ureter, or at least to suggest the anomaly from distortion of the upper pole.

In 3 of their cases the condition was unilateral and in 1 bilateral. All were females. All were cured by heminephro-ureterectomy.—*W. C. MacCarty, Jr., M.D.*

Holmes, R. Brian. Primary tumors of the ureter: their roentgen diagnostic features. *Radiology*, April, 1951, *56*, 520–527.

Seventeen primary ureteral carcinomas of varying grades of malignancy and 1 hemangioma are reported.

Hematuria was present in 94 per cent of the patients. They may also have pain, weight loss, frequency of urination and dysuria.

Plain roentgenograms may reveal enlargement or alteration of the kidney shadow due to hydronephrosis. An excretory urogram demonstrated failure of excretion on the involved side in 71 per cent of the patients. In the remainder, there was a delayed excretion of the medium into a dilated calyceal system. The ureter above the lesion was usually dilated and sometimes tortuous.

Visualization of the ureter by retrograde injection of contrast medium offers the greatest opportunity for diagnosis. Irregular or nodular filling defects may project into the lumen. Obstruction to the retrograde flow of contrast medium will disclose a sharp cut-off at the top of the radiopaque column. There may be an obstructing mass which enlarges the lumen of the ureter but permits the medium to flow partially around it, thus outlining its lower portion.

If non-opaque filling defects are seen near ureteral calculi the diagnosis of tumor must be considered.

Ureteral tumors must be differentiated from non-opaque calculi, blood clots and stricture.—*E. E. Seedorf, M. D.*

Beatty, Ralph P., and Wright, Alfred E., Jr. Cancer of the prostate gland; a fourth interim report. *Urol. & Cutan. Rev.*, April, 1951, *55*, 199–203.

In this paper the authors present a report of 138 patients with prostatic carcinoma, covering a seven year period from 1942 to 1948. The age incidence is approximately the same as that for benign hyperplasia of the prostate. Seventy-five per cent occurred in the seventh and eighth decades. The onset is usually insidious and the disease rather advanced by the time it is diagnosed. Treatment is directed toward relief of obstruction, amelioration of pain, and measures to improve the health and well being of the patient. Bilateral orchiectomy, stilbestrol, and transurethral resection are usually carried out in the individual case.

Of the 138 cases, 24 have survived to the present date of writing; 74 patients were lost from observation and are assumed to have died from their disease. Five patients who failed to respond to the questionnaire sent out were not included in this series.

As a result of the survey the authors conclude that the management of this disease presupposes early recognition and employment of every therapeutic aid in the armamentarium.—*G. W. Chamberlin, M.D.*

## Skeletal System

Buetti, C. Zur Darstellung der Atlanto-epistropheal-Gelenke bzw. der Procc. transversi atlantis und epistrophei. (On the demonstration of the atlanto-epistropheal joint and the transverse processes of the atlas and epistropheus.) *Radiol. clin.*, May, 1951, *20*, 168–173.

Clear roentgen visualization of the atlanto-axial joint, of the transverse processes of the atlas and axis and particularly of the atlanto-occipital joint is a difficult task due to superimposition of shadows cast by the adjacent bones. Usually, roentgenograms are necessary in the following views: (1) posteroanterior view with the patient's mouth closed, when the aforementioned structures are projected into the maxillary sinuses; (2) transorbital anteroposterior oblique view which often is unsatisfactory owing to the superimposed shadows of the maxillary sinuses and orbits; (3) posteroanterior view with the patient's mouth closed when the above structures are projected into the space between the mandible and the maxilla; and (4) anteroposterior view with the mouth open which, however, leads to successful exposures only when the lower occipital contour is exactly level with the line of the upper teeth or with the hard palate of the toothless individual.

In patients with complete or nearly complete upper and lower dental rows, neither the posteroanterior nor the anteroposterior views through the open mouth permit entire elimination of the shadows of the superimposed upper teeth. In such instances, the author often obtained good visualization by using the open mouth technique in the anteroposterior view with an oblique, instead of a straightforward, positioning of the head.

The following is the author's procedure: the patient lies on his back but turns his head to one or the other side respectively, until the sagittal plane of the skull forms an angle of 45–50° with the top of the roentgenographic table. With the patient's mouth wide open, the roentgen beam is directed perpendicular to the top of the table and centered on the corner of the mouth of the opposite side, so that the point of emergence is at the tip of the mastoid process on the side to be examined.

Beautiful roentgenograms of a normal person and 2 patients with pathologic lesions are reproduced to illustrate the value of the method in well selected cases.—*T. Leucutia, M.D.*

McManis, Thayne F., and Dehne, Ernst. Infantile ankylosis of the temporomandibular joint; treatment by resection of mandibular condyle. *J. Bone & Joint Surg.*, April, 1951, *33-A*, 505–507.

When ankylosis of the temporomandibular joint occurs in the infant, it not only prevents opening of the mouth, but leads to marked distortion of the face by growth deformity and atrophy of the disused muscles as the child develops. In the case reported, the authors felt that the growth center had already been considerably damaged and that its preservation was of questionable value. The patient was a girl, eight years old, with deformity of the face. There was marked asymmetry of the lower third of her face with deviation of the chin to the right and flattening and depression of the jaw on the left. In spite of opinion that resection of the condyle at an early age will result in destruction of the growth center, the patient was operated upon. The postoperative course indicates that restoration of normal function decreased the deformity and stimulated the eruption of a retarded tooth. The authors emphasize the necessity of close cooperation between the dental surgeon and the orthopedic surgeon in the treatment of these cases.—*R. S. Bromer, M.D.*

De Vulpian, P., Kirsch, J., and Levrel, P. Une ostéopoecilie familiale. (A case of familial osteopecilia.) *J. de radiol. et d'électrol. & Arch. d'électric. méd.*, 1951, *32*, 465–469.

During the course of interpretation of a chest roentgenogram of an eighteen year old girl afflicted with pulmonary tuberculosis the authors accidentally discovered the presence of osteopecilia. They then made a roentgenographic study of the entire skeleton in the patient examined and of the hands of 15 members of her family. The findings are given in the present article. It was established that the mother, a brother, a sister, a nephew and a niece (these latter two being the children of the oldest sister who herself was not affected) also had osteopecilia, thus confirming the familial nature of the anomaly.

Based on this observation and on pertinent data collected from an extensive review of the literature, the authors discuss the history, clinical course, roentgen appearance, pathologic anatomy and pathogenesis of osteopecilia.

They arrive at the following conclusions: (1) Osteopecilia is usually discovered in an accidental manner. (2) The only manifest sign is the characteristic roentgenographic appearance. The persons affected with osteopecilia have no clinical symptoms or disorders of any kind. (3) In children the lesions may be so small that they may be completely missed at fluoroscopic examination. (4) The anomaly is familial and hereditary. (5) The authors do not believe that osteopecilia occurs more frequently in tuberculous individuals, despite the fact that their patient on whom the original observation was made had pulmonary tuberculosis. (6) After weighing all the facts, they express the opinion that osteopecilia is the result of a congenital anomaly of the osseous structure.—*T. Leucutia, M.D.*

Wise, Robert E., and Weiford, Edward C. X-ray visualization of the intervertebral disk. *Cleveland Clin. Quart.*, April, 1951, *18*, 127–130.

The technique described by Lindblom is used. One short fine gauge lumbar puncture needle is inserted into the spinal canal. Through this needle, another smaller gauge longer needle is introduced across the spinal canal into the center of the disc. The position of the needle is checked fluoroscopically. When found satisfactory, 2 cc. of 35 per cent diodrast is injected, the needles removed and roentgenograms made. If the disc is normal the contrast medium remains localized. In a ruptured disc the contrast medium is dispersed and often extrudes posteriorly.

The technique has been employed in 43 cases. Twenty-one of these patients have been operated upon and the protrusion demonstrated by the roentgenogram has been disclosed in every instance.—*V. L. Peterson, M.D.*

Gillespie, H. W. Vertebral retroposition (reversed spondylolisthesis). *Brit. J. Radiol.*, April, 1951, *24*, 193–197.

Since the condition was described in 1934, the subject of vertebral retroposition has been controversial. It has been variously described as a rare occurrence, a common abnormality, seen in 10 per cent of cases, and an optical illusion. The author found the condition to exist in 77 cases out of a series of 493 patients with surgically proved intervertebral disc protrusions. He examined 35 of these 77 cases and found the backward displacement to vary between 0.3 cm. and 0.9 cm. These were all retroposition of the fifth lumbar body or the sacrum, but the condition is also seen in the cervical and less often in the thoracic regions. Variations in position of the patient and the roentgen tube can exaggerate or

minimize the deformity, but cannot eliminate it. The appearance of retroposition can be produced, however, by incorrect positioning of the patient.

The mechanism of retroposition has been described. When the posterior intervertebral facets are in a frontal plane, the position is unstable, and backward slipping is possible. With marked reduction of the disc spacing, retroposition may take place with a parasagittal disposition of the facets. In 30 of 35 of the author's cases, the points were in a frontal plane. The same percentage of cases was found to be associated with a narrowed intervertebral disc spacing at the same site, and this was thought to be the significant part of the study. While the author feels that retroposition itself is not a sufficient cause for backache, it is a useful indication of disc changes which may be the cause of clinical manifestations.

Causes for retroposition other than disc changes are rheumatoid spondylitis, infection, as tuberculous or pyogenic, trauma, or a congenital abnormality.—*E. F. Lang, M.D.*

Mazet, Robert, Jr. Vertebral manifestations of malignant lymphoma, myeloid leucemia, and multiple myeloma. *Surgery*, April, 1951, *29*, 545–554.

Osseous manifestations of malignant diseases of the reticuloendothelial tissue are commoner than is generally supposed or than is demonstrable by roentgenograms. The author expresses the opinion that involvement of bone is an early, rather than a late, occurrence in these conditions. Roentgenograms more frequently show osteolytic lesions but may disclose osteoblastic or periosteal reactive lesions. Osseous involvement is demonstrable on roentgenograms only if there is extensive affection of the spongiosa, or destruction of the cortex.

Specimens collected at necropsy in a series of cases of Hodgkin's disease exhibited osseous lesions much more frequently than they were shown by clinical or roentgenologic methods. Steiner collected 2,006 cases, of which 8.3 per cent showed clinical evidence of lesions of bone. Necropsy had been performed in 547 of these cases and 28.3 per cent exhibited osseous lesions. Falconer and Leonard found definite involvement of bone in 14.9 per cent of 750 cases of Hodgkin's disease studied roentgenologically. At necropsy, osseous lesions were found in 53.3 per cent of 213 cases. In the author's smaller series of 28 patients with Hodgkin's disease, 17.8 per cent were found to have osseous lesions demonstrated roentgenographically. At necropsy, however, osseous involvement was noted in 71.4 per cent. The higher percentage of osseous lesions found at necropsy is attributed to the fact that the pathologists were seeking such lesions more diligently in the author's series.

In the author's series, when any other bone was involved, the vertebral column invariably showed changes. Needle biopsy of vertebral lesions of questionable nature was found to be a valuable procedure.—*P. G. Dillard, M.D.*

Lachapèle, A. P., and Lagarde, Claude, with the collaboration of Texier, R., and Duluc, J. De la spondylolyse (étude radio-clinique de 93 observations personnelles). (Spondylolysis; roentgenological-clinical study of 93 personal cases.) *J. de radiol. et d'électrol. & Arch. d'électric. méd.*, 1951, *32*, 453–464.

As the subtitle indicates the authors present their personal observations in 93 cases of spondylolysis. They give detailed statistical data on the incidence, site, age, sex, etiology, clinical manifestations and roentgen features of the anomaly.

In view of the medicolegal aspect involved, the possible etiologic and pathogenic factors were studied with particular care. In 10 cases (10.7 per cent) there was evidence of direct trauma either in the form of a severe single blow or repeated small injuries. Thirteen persons gave a history of trauma but the evidence was indefinite. These cases represented the most difficult problems from the medicolegal standpoint and, in case of doubt, usually obtained favorable decisions. In the remaining 70 persons, no trauma of any kind was present.

The authors, therefore, arrive at the conclusion that spondylolysis constitutes a malformation of the posterior vertebral arch of a hereditary degenerative nature, in which trauma has no other role than that it leads to its discovery or to its aggravation.

The article is well illustrated with reproductions of beautiful roentgenograms and many schematic drawings.—*T. Leucutia, M.D.*

Gall, Edward A., Bennett, Granville A., and Bauer, Walter. Generalized hypertrophic osteoarthropathy; pathologic study of seven cases. *Am. J. Path.*, May–June, 1951, *27*, 349–381.

The association of digital clubbing with intrathoracic disease has been recognized since antiquity. The wider distribution of the lesions with involvement of the shafts of the larger bones of the extremities has been appreciated only comparatively recently. The syndrome termed generalized hypertrophic osteoarthropathy may be defined as that condition occurring as a sequela of some major visceral disorder, usually intrathoracic in location which is manifested by clubbing of the digits and ossifying periostitis, mainly of long bones, and is frequently associated with joint symptoms.

The specimens serving as the basis for this study were obtained for biopsy or at necropsy from 7 men ranging in age from eighteen to sixty-five years. Six patients had severe pulmonary disease and 1 had congenital heart disease. No precise explanation for the mechanism underlying the varied skeletal and soft tissue lesions of the syndrome is available.

Physical signs and symptoms of hypertrophic osteoarthropathy are extremely varied. In the majority of cases, widening of the terminal portions of the fingers and toes, with or without excessive curvature of the nails, is the first abnormality noted. Many patients complain or intermittent pain and tenderness along the extremities. Stiffness and tenderness of the peripheral joints are frequently observed. Not uncommonly, signs and symptoms pointing to the presence of the skeletal changes may antedate those referable to the primary visceral disease.

The anatomical findings aid one in explaining the varied clinical manifestations. The clubbing of the fingers and toes is due to an increase in the bulk of the soft tissues around the terminal phalanges and beneath the nails. Hyperemia, edema, increased amounts of loose connective tissue, and mild chronic inflammation are the predominant features of the lesion.

The osseous lesion begins as a low grade inflammatory reaction in the periosteum. This is followed by abundant subperiosteal new bone formation with centrifugal displacement of the thickened periosteum. The periosteal changes are usually observed first along the distal third of the bones of the forearm and leg. Progression is usually toward the proximal portions of these bones. Later, similar lesions appear along the lower ends of the femur and humerus, and still later the shafts of the metacarpals, metatarsals and occasionally of the phalanges may be involved. The pseudocortex formed ultimately fuses with and expands the original cortex, and during the course of fusion the original cortex exhibits resorption and adaptation to increased shaft diameter.

Articulations in the involved extremities are the seat of mild to moderately severe chronic synovitis associated with nonspecific degenerative changes in the articular cartilages.

Illustrations demonstrating the roentgen appearance of the bony changes and also several microscopic sections of involved bones and joints are included.—*A. B. Smith, M.D.*

Allende, Guillermo, and Lezama, Luis G. Fractures of the neck of the femur in children; a clinical study. *J. Bone & Joint Surg.*, April, 1951, *33-A*, 387–395.

Fractures of the neck of the femur are rare among children when the frequency with which they occur among adults is taken into consideration. The complications and prognosis vary according to the type of fracture. The two essential factors with which the surgeon must be concerned are the obliquity of fracture line and the possible appearance of aseptic necrosis. The authors had under their care 8 children with fractures of the neck of the femur, the youngest being eight years old and the oldest fourteen. Each fracture was the result of severe trauma and some of them were associated with other fractures—fracture of the pelvis, fracture of the humerus and fracture of the skull.

In those cases where the angle of inclination was less than 50 degrees, it was found that reduction under general anesthesia and immobilization for two months in the Whitman position constituted the treatment of choice.

When the Pauwels angle was greater than 50 degrees and the displacement of the fragments was not too great, an intertrochanteric osteotomy modifying the direction of the fracture line was sufficient to obtain consolidation, although the final result was nearly always a coxa vara. The authors found that, when displacement was pronounced, and the fracture was not a recent one, it was better to use a fibular graft with an intertrochanteric osteotomy. This graft, when introduced into the fragments of the metaphysis, produces a lever movement which raises the head and prevents varus of the neck, according to the method of Mayer.

In only 2 of the cases was there the complication of aseptic necrosis. The frequency of this sequela is due, in great part, to the condition of the vessels supplying the neck of the femur. The center of ossification of the head of the femur does not reach full development until the child is between eleven and thirteen years old, at which time the foveolar arteries become anastomosed with the retinacular arteries. After this has occurred, there is a greater possibility that together these vessels will supply the necessary circulation to the fractured neck. It is this developmental background of blood supply which accounts for the greater frequency of aseptic necrosis in children than in adults. The authors feel that when the Pauwels angle is greater than 50 degrees a prompt osteotomy is fundamental to solid bony union. The process of consolidation can be accelerated by the use of a fibular graft combined with the osteotomy.—*R. S. Bromer, M.D.*

Lacroix, Pierre, and Verbrugge, Jean. Slipping of the upper femoral epiphysis; a pathological study. *J. Bone & Joint Surg.*, April, 1951, *33-A*, 371–382.

The pathology of the slipping of the upper femoral epiphysis was studied, the material being whole sections of the diseased area from 2 cases. Based on the histopathological evidence, the primary cause lies in the epiphyseal cartilage which, instead of producing endochondral bone, is transfored into fibrous tissue. All the other lesions found in the neck and head are secondary. The authors believe that trauma may reveal the disease or may complicate it by causing an acute slipping, but it cannot be considered a primary cause of the lesion. They feel that so far the endocrine theory of causation of the lesion has nothing more to support it than a mere clinical suggestion. All hypotheses such as a weakening of the periosteum, a low grade infection, circula-

tory disturbances, late rickets or a localized osteomalacia, are ruled out by observation of the pathological changes.—*R. S. Bromer, M.D.*

Massie, William K. Vascular epiphyseal changes in congenital dislocation of the hip; results in adults compared with results in coxa plana and in congenital dislocation without vascular changes. *J. Bone & Joint Surg.*, April, 1951, *33-A*, 284–306.

The existence of vascular impairment of the epiphysis of the femur following the reduction of a congenitally dislocated hip has long been recognized. The author states the purpose of his paper is to tabulate the early roentgenographic findings considered pathological in the light of subsequent adult deformities; to reiterate the significance of clinical findings at maturity, when compared with results in a group of 15 adults with congenitally dislocated hips, but without vascular changes; to illustrate the close similarity between congenital dislocation and coxa plana, and to compare the two conditions in the adult, both clinically and roentgenographically.

In his discussion of the roentgenographic findings, Massie lists the salient changes of three groups, based on degree of severity of the changes, and a fourth or mixed group which was composed of hips showing early, definitely abnormal epiphyseal changes, but lacking the fragmentation of the epiphysis characteristic of both the involved group and of typical coxa plana.

In his summary he states the poor results in the treatment of congenital dislocation of the tip stem either from resubluxation after reduction or from the onset of vascular changes in the epiphysis. The former is preventable by treatment. The occurrence of vascular changes in hips reduced after one year of age, however, at present is neither predictable nor preventable. In the series reported, 35 per cent showed definite vascular changes and another 20 per cent had a roentgenographic appearance indicating partial involvement; in 72 of the hips involved by such changes adult results were unsatisfactory. Clinically these patients are distinguishable by persistent symptoms at an early age. The changes are considered identical to those of coxa plana manifested at an earlier age. When left untreated, however, they result in more severe adult deformity. A comparably high male sex incidence was noted in both groups of hips. Massie postulates a susceptibility to vascular injury on the basis of individual variations in the vascular supply to the femoral head. The importance of early recognition for treatment of this disorder cannot be stressed too much. The method of treatment which he advocates at this time is prohibition of weight-bearing until the head appears healed roentgenographically.—*R. S. Bromer, M.D.*

Minear, W. L. Xanthomatous joint tumors. *J. Bone & Joint Surg.*, April, 1951, *33-A*, 451–458.

In this paper 5 cases of joint xanthoma are reported. This brings the total of cases reported in the literature to approximately 81. Synonyms of the condition are numerous; some of the terms used are "pigmented villonodular synovitis," "villous arthritis of the knee" and "hemorrhagic villous arthritis of the knee." Other designations commonly employed are xanthogranuloma and giant cell tumor.

Joint xanthoma is suggested by the presence of a chronic mono-articular lesion, often a palpable tumor, of the knee or ankle. Roentgenographic examination in many cases is reported in the literature as negative, but in those of long standing, there may be moderate decalcification of bone and erosion from tumor pressure. In the first case reported in this paper, the lateral view of the knee showed the xanthoma filling the anterior and posterior compartments and the suprapatellar pouch. The osseous structure was characterized by slight coarsening of the trabeculations consistent with bone atrophy. Aspiration produces sterile serosanguineous exudate, sometimes laden with cholesterol. The true nature of the xanthoma tissue is unknown.—*R. S. Bromer, M.D.*

Moore, Sherwood. Osteitis deformans; a theory of its etiology. *J. Bone & Joint Surg.*, April, 1951, *33-A*, 421–430.

In this paper the incidence, symptomatology, skeletal distribution, laboratory findings, complications, pathology and treatment of Paget's disease of bone are described. In his discussion of the cause of osteitis deformans, Moore mentions writers who have noted the great enlargement of the temporal arteries when the skull was affected. In operations on pagetoid bone, surgeons have encountered marked and troublesome vascularity. Measurements of the volume flow of blood to normal bone and to bone of Paget's disease show that, according to Edholm, Howarth and McMichael, it was up to twenty times greater in the latter than the former. Several observations in the literature firmly establish the fact that there is a close relationship between Paget's disease and disturbance of the circulation. This suggests that there is a circulatory factor in the production of the disease; when the process is widespread, the heart will suffer.

In the summary of the paper a hypothesis as to the etiology of osteitis deformans is based on the fact that the blood circulation is profoundly altered. A cause of the increased vascularity must be sought for. The autonomic nervous system controls the blood vessels, increasing or decreasing the volume flow of blood, subject to various influences. It is proposed that disorder, either organic or functional, of the autonomic nervous system brings about the

increased vascularity of the bone in osteitis deformans. This theory can account for the increased volume flow of blood to the involved bone, the stage of bone resorption, the stage of bone repair, the increased growth of bone, and also the local thermogenesis, which is the product of heightened metabolic exchange. In no other way can the phenomena of osteitis be explained. Moore therefore proposes that osteitis deformans is actually due to sporadic failure of the autonomic nervous system and is not a disease of bone. However, this does not explain the absence of comparable changes in the adjacent soft tissues.—*R. S. Bromer, M.D.*

Strassburger, Paul, Garber, C. Zent, and Hallock, Halford. Fibrous dysplasia of bone. *J. Bone & Joint Surg.*, April, 1951, *33-A*, 407–420.

Fibrous dysplasia is a clinical syndrome that may present itself in various ways. Patients with the disease may be divided into three groups: first, those with single or multiple lesions in one bone; second, those with lesions in several bones, with or without skin pigmentation; third, those with multiple bone lesions, dermal pigmentation (of the café au lait type), and precocious puberty, either alone or in association with early skeletal maturation. The etiology of fibrous dysplasia is unknown.

The authors have had experience with 9 cases. In adults there may be rather extensive lesions in more than one bone without symptoms or impairment of function. The solitary lesions respond to curettage and packing with bone chips, but this procedure in their experience was not beneficial in treating large lesions, where abnormal tissue could not be entirely removed.

The roentgenographic findings are variable and the bone lesions are usually insidious in onset. The earliest manifestations are areas of decreased density within the cortical structure with a rather diffuse ground-glass appearance. These are not cysts, but areas in which bony trabeculae have been replaced with fibrous and osteoid tissue, the density of which is less than that of normal bone. At times the lesions show a more diffuse appearance with areas of both decreased and increased density.

As the lesions progress, the involved areas increase in size and in many instances expansion and thinning of the cortex occur, accompanied by local osteoporosis and bowing of the bones. A great deal of variability exists in these lesions and they do not all progress; many remain static for years.

The differential diagnosis from hyperparathyroidism, sarcoid, Paget's disease, multiple myeloma, skeletal enchondromatosis, lipoid granulomatosis, bone cyst and giant cell tumor is discussed. When islands of cartilage are found, the diagnosis can be made on the basis of the gross or microscopic examination alone.—*R.S. Bromer, M.D.*

Ellis, John T., and Barr, David P. Metastasizing carcinoma of the parathyroid gland with osteitis fibrosa cystica and extensive calcinosis. *Am. J. Path.*, May–June, 1951, *27*, 383–405.

The case described in this paper provides one of the few examples of metastasizing carcinoma of the parathyroid gland studies postmortem. Osteitis fibrosa cystica and extensive calcinosis were the outstanding findings. The tumors removed surgically from the neck and lung and those found postmortem in the sternocleidomastoid muscle and liver were alike in histopathologic appearance. They were composed for the most part of well differentiated cells which by morphologic criteria could not be distinguished from the elements of growths generally diagnosed as parathyroid adenomas.

Three remaining parathyroid glands were neither neoplastic nor hyperplastic, but showed fibrosis and atrophy. The possibility was considered that this may have been an involutionary change resulting from hypersecretion of parathyroid hormone by the neoplastic cells.

Osteitis fibrosa cystica was generalized but less extensive than in a number of previously reported cases of hyperparathyroidism.

Other features were a very marked degree of medial calcification of arteries of medium and small size, associated clinically with pallor, cyanosis and circulatory insufficiency of the extremities; extensive deposition of calcium in infarcted areas of the lungs; widespread renal calcinosis without obvious nephrolithiasis or renal failure; and metastatic calcification of the gastric mucosa, which was not limited to cells engaged in acid secretion.

Seven plates showing roentgen findings in the lungs and gross and microscopic pathology in various organs are attached.—*A. B. Smith, M.D.*

Blair, Harry C. A diamond-shaped graft from the ilium for non-union of the tibia. *J. Bone & Joint Surg.*, April, 1951, *33-A*, 362–370.

The procedure presented in this paper consists of taking a diamond-shaped graft from the ilium for non-union or delayed union of the tibia. To commend it, the author states, are ease of execution and the subsequent rapid healing. The method is based on the presumptions that fresh longitudinal fractures of long bones tend to heal quickly, that cancellous bone from the ilium is more osteogenic than tibial cortex, and that pressure contact of a physiological nature aids in osteogenesis. Neither screw nor tie fixation is used.

A linear fracture is made in each tibial fragment to form the bed for the diamond-shaped graft from the ilium. These have all the attributes of fresh fractures of the long bones sustained accidentally. Like other linear or oblique fractures of long bones,

which seldom show delayed union, they heal quickly. Probably contributing to the healing is the copious supply of fracture pabulum furnished by the exposure of large areas of newly fractured bone. Furthermore, the healing power of these, as well as of other fresh fractures, is greatest in the first few weeks following injury. When the subsequent contraction of the connective tissue begins and fibrosis takes place, the ability to form bone lessens. Roentgenograms are shown illustrating results of this method.—*R. S. Bromer, M.D.*

Kelly, Robert P., and Murphy, Fred E. Fatigue fractures of the tibia. *South. M. J.*, April, 1951, *44*, 290–295.

The authors report 2 cases of fatigue fracture of the tibia and present a rather complete review of the literature.

The concept of fatigue fracture of bone is not different from that implied by the same term applied to other physical substances. It is that a basically sound material undergoes mechanical dissolution in response to prolonged concentration of strain on a localized area. In the evolution of mechanical or structural parts, design is altered in deference to demonstrated habitual tendency to breakage at a constant point in response to more or less prolonged use. Known march fracture of the metatarsal is believed to be of the same type.

Although the exact etiology of this type of fracture is not definitely known, the authors feel that it is produced by repetitious microtrauma without systemic disease as the etiologic background. However, there are those who feel that systemic disease does play a part in the production of this lesion. Others feel that the lesion develops as the result of an isolated injury severe enough of itself to produce a fracture without displacement but not recognized by the patient. The suggestion has been made that this condition represents an obscure infection. The lesion has not been considered to represent a neoplasm, though until the individual case is placed in the correct category its differentiation from neoplasm must frequently be made. No cases have been presented to substantiate the possible etiologic factors as mentioned above.

The literature contains reports in some detail of 41 instances of fatigue fracture of the tibia. Of the number, 4 presented bilateral lesions making a total of 45 tibiae. The condition occurred most frequently in the younger age group, the age varying from four to twenty-three years. In 37 cases, it was observed in the upper third of the tibia; in 3 in the middle third, and in 3 in the lower third. Tenderness has been recorded as present in 13 cases and as absent in 1 case. Swelling was noted in 16 cases and absent in 8. Increase in temperature was found over the site of the lesion in 5 cases. Pain on activity was present in 23 cases.

The roentgenographic features are not entirely characteristic. In general, callus is seen frequently medially and posteriorly and occasionally laterally. There may be a line of infraction of the medial cortex early in the course of symptoms. Those reporting the major groups of cases agree that a line of infraction through the cortex medially and posteriorly is frequently seen later. One author has emphasized the transverse radiopaque zone across the medullary space and notes that it is occasionally penetrated by a hair-like radiolucent line.

Two cases are presented in considerable detail. There are numerous roentgenograms.—*J. G. Snead, M.D.*

Jordan, Henry H., and Brodsky, Alexander E. Keller operation for hallux valgus and hallux rigidus; an end result study. *Arch. Surg.*, April, 1951, *62*, 586–596.

Of interest to roentgenologists is the high percentage of good results reported in this paper. Of 161 operations, a result satisfactory to both patient and surgeon was obtained in 159; and the authors attribute the two unsatisfactory results (partial ankylosis and pain in the first metatarsophalangeal joint) to poor surgical judgment—removal of insufficient proximal phalanx. In all cases, relief was sought for pain and not for cosmetic reasons alone, and the hallux valgus or hallux rigidus had been present more than five years. The average follow-up period was three and one-half years and in no case less than one year.

Except for the occasional congenital hallux valgus, the authors regard the deformity and hallux rigidus as the result of foot pronation, with incorrect footwear serving to aggravate a mild or potential deformity. Walking with the tarsus in pronation increases the weight bearing thrust through the first metatarsal and great toe. The result, as seen in roentgenograms, is familiar. There is the hallux valgus deformity, degenerative arthritis of the first metatarsophalangeal joints and enlargement of the first metatarsal heads with baring of the medial portions of the heads which no longer articulate with the bases of the proximal phalanges.

In the Keller operation, the deformity is corrected by shortening the skeleton of the great toe (at least two-thirds of the proximal phalanx is removed). The authors describe other less important steps in the operative technique and discuss the handling of associated deformities and symptoms.—*George Cooper, Jr., M.D.*

Gellman, Moses. Fractures of the anterior process of the calcaneus. *J. Bone & Joint Surg.*, April, 1951, *33-A*, 382–386.

It is the author's belief that fractures of the anterior process of the calcaneus are relatively rare or are frequently overlooked. The manner in which this

fracture is sustained may vary, but the cause is commonly believed to be forcible adduction of the forepart of the foot, combined with plantar flexion. The precise location of a trigger point aids in the diagnosis, which must be confirmed by careful roentgenographic observations The routine anteroposterior view of the foot is seldom helpful. A direct lateral exposure is not always sufficient to demonstrate this fracture, especially if the fracture line throws only a faint shadow, or if there is no appreciable displacement of the fragment. Oblique views at several different angles must be made in order to separate the shadow of the anterior process of the os calcis from that of the front and under surfaces of the talus. Unless suspected and scrupulously sought, minute fractures at this site are often unseen and remain undiagnosed; hence they are improperly handled.

While the disability is prolonged, the prognosis is good. Gross displacement may be corrected by manipulation. A simple below-the-knee cast gives comfort in the more severe cases, an elastic bandage is sufficient in the less severe cases.—*R. S. Bromer, M. D.*

### Blood and Lymph System

Scott, Wendell G. The development of angiocardiography and aortography. Carman Lecture. *Radiology*, April, 1951, *56*, 485–519.

In presenting the Carman Lecture, Scott pays tribute to Dr. Russell David Carman on the anniversary of his seventy-fifth birthday.

The historical development of diagnostic roentgenologic achievements leading to the maturing of angiocardiography is reviewed.

The present choice of contrast media is limited to 70 per cent diodrast, 75 per cent neo-iopax, and 70 per cent urokon. Undesirable reactions and occasional death may follow the injection of these media. Patients with renal complications, those who are extremely debilitated and those known to be hypersenstitive to the drug should not be subjected to this examination.

There is a comprehensive description of the various types of equipment used for angiocardiography. These include photofluorography, fast continuous cassette changers, attachments for rapid direct roentgenography on large roll film, double or twin roentgenographic apparatus for two-plane right-angle roentgenography, and some special accessories such as fast timers and sequencing devices. The purpose is to obtain usually two to six exposures per second as the opaque medium rapidly passes through the vascular field.

The greatest value of angiocardiography has been in the diagnosis of congenital malformations of the heart and especially in the accurate detection and selection of those who are amenable to surgical correction. It is applicable to about half of the individuals afflicted with these disorders who are admitted to the hospital for further diagnosis and appraisal and to a little less than half of those who undergo corrective surgical measures. The conventional methods of examination are usually satisfactory in about 50 per cent of the cases and should always be done first.

Twelve case reports of malformation of the heart and great vessels are presented. Angiocardiograms of these cases demonstrate pertinent anatomical variations which are not revealed on conventional films.

The satisfactory application of angiocardiography and aortography to the diagnosis of congenital heart lesions has brought about a better understanding of these disorders and at the same time a wider dissemination of knowledge about them. This has been a great help in the more effective use and interpretation of conventional fluoroscopic and roentgenographic examinations on this group of patients.

Retrograde aortography is a second method for visualization of the aorta and its main branches. Several approaches are mentioned, but the author has selected the left common carotid artery as the most convenient route. Under general anesthesia, the artery is exposed, and 20 to 40 cc. of a 70 per cent contrast medium are injected very rapidly while the roentgen exposures are continued for four or five seconds.

The retrograde method gives a much higher concentration of the opaque material in the aorta and eliminates the obscuring shadows of the overlying chambers of the heart and pulmonary vessels. The procedure has been helpful in the better visualization of the site, extent and length of coarctations of the aorta, in the positive demonstration of patent ductus arteriosus, in anomalies involving the arch of the aorta and its major branches, in the differentiation of aneurysm and mediastinal tumors, and in visualizing the coronary arteries.

Some of the disadvantages of the retrograde method are that the surgical exposure of the artery necessitates the use of the operating room and there is a resulting scar after closure. The hazard of incurring complications is also greater.

There are 16 excellent figures and a large selected bibliography concerning the subject.—*E. E. Seedorf, M.D.*

Dotter, Charles, Steinberg, Israel, and Ball, Robert P. Angiography. *Circulation*, April, 1951, *3*, 606–615.

The general subject of angiography may be classified into four regional categories, as follows; (1) the head, (2) the chest, (3) the abdomen and (4) the extremities. The authors warn against indiscriminate employment of angiography because the intravenous use of the commonly employed contrast media is potentially injurious or even lethal.

The physiology of the circulation must be considered to obtain satisfactory angiograms. The timing

of exposures is more critical during arteriography than venography. Serial rapid roentgenograms during the passage of the contrast medium are necessary in angiocardiography and cerebral angiography.

Diodrast and neo-iopax have been employed commonly and have resulted in less toxic effects than thorotrast and sodium iodide. While the injection of the former iodine compounds in dilute (20 to 40 per cent) or concentrated (70 to 75 per cent) strength is usually painless, spasms and pain may result during arteriography when extravasation occurs.

A variety of successful techniques for peripheral venography have been published. The most commonly employed method consists of the injection of the contrast medium into a vein distal to the area of investigation. A tourniquet about the leg at the knee may result in better filling of the deep veins. If the deep veins are demonstrated, they are patent. The opposite is not always true. For study of the patency of the valves of the femoral and saphenous veins, the injection of 10 cc. of contrast medium in the femoral vein near the inguinal ligament with the patient in semi-erect posture is usually satisfactory. Venography of the arms is similar to that of the leg except that rapid injection is preferable.

Arteriography of the extremities may be direct or indirect. Direct arteriography consists of the rapid injection of from 10 to 15 cc. of the dilute contrast medium in the direction of the blood flow. Films should be made immediately at the end of the injection. Rapid serial exposures during and shortly after injection at the rate of one or more per second have given excellent results. Retrograde arteriography with occlusion of the artery above and the catheterization of the artery are additional methods of investigation in selected cases. Arteriovenous aneurysms, obliterative arterial disease, emboli, injuries and their surgical repair and malignant bone tumors may be studied by means of peripheral arteriography. Giant cell tumors, for example, show vascularity around their periphery while malignant bone tumors usually show pooling of contrast medium within the tumor.

In abdominal aortography a general anesthetic is administered to the patient in the prone position. A 15 cm. long, 18 gauge needle with stylet is inserted into the aorta with skin puncture below the twelfth rib and 5 cm. to the left of the spinous process. After removal of the stylet and a trial injection of saline from 10 to 15 cc. of the contrast medium (concentrated) is injected. Retrograde filling of the aorta by catheterization of the femoral artery or forcible injection below has been employed but the techniques are more difficult than translumbar puncture.

The iliac veins and the inferior vena cava may be studied by injection into the malleolar vein with the patient in the Trendelenburg position. This technique is of value in demonstrating thrombotic or neoplastic occlusion of the inferior vena cava or iliac veins. The cardiac catheter may be employed for visualization of the hepatic and renal veins. Portal venography at the time of exploration prior to the resection of the pancreas for malignant disease may be of value to demonstrate the extent to which the portal vein has been involved by the tumor.—*J. N. Ané, M.D.*

Dow, J. D. The venographic localisation of incompetent communicating veins in the leg. *Brit. J. Radiol.*, April, 1951, *24*, 182–192.

Veins in the leg or thigh communicating between the deep and superficial veins are inconstant in number and position. An incompetent communicating vein existing below a point of ligation for varices prevents accomplishment of the desired result, and one existing above the point of ligation leads to rapid recanalization and recurrence of superficial varices. For these reasons demonstration of the position of these communicating veins and their competency is important to the surgeon.

The author uses two methods of injection for venography. In one method, the injection is made in a distal superficial vein with a tourniquet about the leg above the site of a suspected communicating vein. In the second method, the injection is made into the superficial circulation in a retrograde direction. By combining these methods the position of the communicating vein in any part of the leg or thigh can be identified with the greatest accuracy. When there is a localized dilatation of the superficial vein at its junction with the communicating vein, that indicates that the communicating vein is incompetent, and the spurting of blood at this site produces the dilatation. In the absence of such a dilatation the communicating vein is competent

When the injection is made in the thigh, 20 cc. of 35 per cent diodone are used. When the injection is made in the leg 10 to 15 cc. is used. In each case roentgenograms in both the anteroposterior and lateral projections of the injected areas are made.

A total of 75 cases was investigated in this manner, and these were subsequently subjected to operation. Where it was possible to localize the communicating veins at operation and test them for competency, there was a high degree of correspondence between the venographic and operative findings. The method is more efficient in the thigh than in the leg, but in both areas it is more accurate than clinical methods. The use of venography will simplify the surgical treatment of varices, make it more effective, and decrease the incidence of recurrence.—*E. F. Lang, M.D.*

Southam, Chester M., Craver, Lloyd F., Dargeon, Harold W., and Burchenal, Joseph H. A study of the natural history of acute leukemia with special reference to the duration of the disease and the occurrence of remissions. *Cancer*, Jan., 1951, *4*, 39–59.

A review of 173 patients with acute leukemia treated at Memorial Hospital from 1926 through 1948 is presented. The authors found the majority of cases of acute lymphatic leukemia and unclassified acute leukemia occurred in children less than eight years of age. There was a fairly even distribution of cases of acute myeloid leukemia in all age groups.

Sixty-six per cent of the cases were in males, and this sex difference was observed quite consistently in all age groups and in all types of leukemia.

The duration of the disease from the onset of symptoms to death ranged from one to fifty-two weeks. The average duration in 150 cases was 20.2 weeks and the median duration 17 weeks.

There appeared to be no relation of age and sex to survival time. The data indicated that endogenous sex hormones do not have any significant influence on the course of the disease and suggested that the sex difference in incidence is due to some non-hormonal factor.

The authors found no significant relation between cytological type and survival time.

Although there was a good indication that supportive therapy and specific therapy, including roentgen ray, radioactive phosphorus, urethane, and nitrogen mustard increased survival time, this was not borne out significantly from a statistical point of view. It must be considered that the great range in survival time in acute leukemia and the resulting large standard deviations necessitate marked prolongation of survival times by any therapeutic method in order to make the change clinically convincing and statistically significant.

In this series of patients there was a progressively shorter survival (from the onset of symptoms) as the degree of leukocytosis increased.

Among the 150 cases treated before the advent of folic acid antagonist, only 13 or (8.7 per cent) showed remissions of any degree. Six of 13 were complete remissions. The average survival time of those patients who had remissions was considerably greater than any other group. None of the patients had more than one remission.

Bone and joint pain was a symptom in 27 (16 per cent) of the patients. Roentgenographic long bone studies were done on 44 patients of whom 23 (52 per cent) showed changes suggestive of leukemic involvement. There was a striking lack of correlation between bone pain as a symptom and roentgenographic bone changes.—*W. L. Bridges, M.D.*

Sylwan, Tore. Percutaneous retrograde phlebography of the leg. *Acta radiol.*, July, 1951, *36*, 66–80.

Phlebography of the leg is usually carried out by injecting 10–20 cc. of an aqueous solution of contrast medium into a peripheral vein and taking roentgenograms proximal to the site of such injection. It is possible by this method to show that the deep veins are permeable. This, at present, is the only definite conclusion that can be drawn from this kind of phlebography (which may suitably be termed centripetal phlebography).

During the year April 1, 1949–April 1, 1950, the author performed a total of 96 retrograde phlebographic examinations with percutaneous injection of contrast medium into the femoral vein. In his conclusions, the author states that pathological changes in the deep veins of the thigh may be shown by means of retrograde phlebography and that this is not possible by any other method of investigation. The essentials required in order that an opinion may be formed are: (1) that roentgenograms of the leg be obtained in at least two right-angled projections; (2) that exposures be made early as the injection of the contrast medium is being carried out; (3) that roentgenograms both of the thigh and the calf be taken. These essentials can scarcely be obtained if the contrast medium is injected into a vessel exposed upon the operating table.

As a result of these 96 retrograde phlebographic examinations the following observations were made: (1) Pathological changes in the deep veins of the thigh appear to be common in chronic venous diseases. (2) Changes have been encountered in the vena profunda femoris as often as in the vena femoralis. (3) The presence of pathological communications with a retrograde direction of flow from the deep to the outer veins of the thigh have been established in addition to the common occurrence of deep varicosities. (4) The site of predilection for anatomical changes is the region around the hiatus adductorius. —*Mary Frances Vastine, M.D.*

Salén, Ernst F. A phlebographic study of constrictive processes in the superior vena cava area and of accompanying changes in the collateral circulation. *Acta radiol.*, July, 1951, *36*, 81–87.

The symptomatology in occlusion of the superior vena cava has been known since the beginning of the 19th Century when it was described by Corvisart. The main features of the clinical picture include stasis in the veins of the neck, arms and thorax and the development of collateral circulation within these vessel paths. In some cases the clinical picture is not characteristic and it is in these instances that it is important to make an exact determination of the degree of stenosis and an estimation of the course of the collateral circulation. Mediastinal phlebography (angiocardiography) in perpendicular planes is valuable in such cases. This was performed by the author in 27 cases of varying degrees of stenosis of the superior vena cava.

Mediastinal phlebography according to this method showed that the stenosis of the vena cava in all the tumors of the lung studied was due to mediastinal

metastases. Severe stenosis of the vena cava was also found in cases of postoperative thrombophlebitis and as a result of systemic diseases such as Hodgkin's disease and lymphosarcoma.

In stenosis of the superior vena cava, the venous backflow may take place in several ways. The azygos system appears to be an important collateral path in man. It seems to become easily adapted to a reversed circulation. The reason for this is not clear. It is possible that the anatomic difference in the structure of the valves may play some role. The valves in the terminal segment of the azygos would then become insufficient or would already be functionally insufficient under physiological conditions.

In the majority of the 27 cases studied it was possible to determine the extent of the stenosis in the superior vena cava. In the other cases, complementary retrograde phlebography was performed by means of a heart catheter introduced from the great saphenous vein via the inferior vena cava and the right auricle. The course of the collateral circulation was shown in 9 cases of severe stenosis.—*Mary Frances Vastine, M.D.*

## General

Shimkin, Michael B. Duration of life in untreated cancer. *Cancer*, Jan., 1951, *4*, 1–8.

The author sets forth an excellent appraisal of reports and literature relative to duration of life in untreated cancer of ten different sites or types. Accurate data of this nature are needed to allow an estimation of prognosis and palliation of the type of therapeutic management for the patient. It is often quite difficult to distinguish between procedures that may retard the progress of neoplasms and purely palliative measures. Only with a yardstick of the survival pattern in untreated cancer patients can one measure the value of treatment designed to cure the neoplasm or produce a prolongation of useful and comfortable life.

The three measuring devices employed to determine duration of life in cancer are: (1) case history, which elicits the date of onset of signs and symptoms first noticed by the patient; (2) medical records, which yield the date of first recourse of the patient to medical aid, date of establishment of diagnosis, and date of initiation of some particular therapy; and (3) death records. It is felt that the time from the date of onset as derived from the patient's history to time of death is the most satisfactory method to use.

The author presents graphs and tables concerning the duration of life reported by several authors for neoplasms of breast, rectum, cervix, oral cavity, stomach, larynx, esophagus, prostate, bladder, and lymphomas. These records should prove useful to the cancer therapist in evaluating the efficacy of treatment methods.

The author also points out the similarity in natural survival statistics taken from different samples of patients by various authors. There is no convincing evidence that the mean age of onset, duration of life, or age at death in the neoplastic diseases common to both sexes are consistently different in the two sexes. Likewise, there is no significant or convincing evidence of increase or decrease in the mean life span of the various groups according to the age at onset, *i.e.*, cancer does not kill faster in young patients than in those of advanced years.—*J. A. Campbell, M.D.*

Masson, P. My conception of cellular nevi. *Cancer*, Jan., 1951, *4*, 9–38.

The author gives a complete discussion of the cellular constituents of pigmented nevi. He presents the differences between "naevi incipientes" of the newborn and the compound and intradermal nevi of adults. The nevi of infants may show one of the three following types: (1) they may be characterized by local overactivity of melanogenesis without increase in melanoblasts, (2) there may be an overproduction of melanoblasts and over pigmentation, and (3) the nevi may develop the characteristics of "compound nevi."

The intradermic "compound nevi" have two distinct origins: One constituent is the epidermic melanoblast which has multiplied and spread into the superficial dermis; and the other element is the Schwann cell, which has multiplied and infiltrated into the deep dermis. As the melanoblasts grow downward and the Schwann cells upward, they meet in the dermis and merge together. The nevus, although derived from two distinct sources, now becomes one single structure. As long as the migration of the melanoblasts occurs, the nevus will remain a compound nevus. When this ceases, the nevus becomes an intradermal nevus.

Whatever the origin of the nevic cells, they share the same property. These properties are the characteristics of the schwannian syncytium. The neuroid symplasm is always neurotized, but never completely. In the author's opinion, all cellular nevi are thus neuronevi, except those that develop in the palmar and plantar regions.

It is not clear as to which constituent gives rise to the malignant melanoma. It is well known that quiescent nevi as well as previously unpigmented areas form the site of a malignant melanoma. From the available material the author, however, is unable to state whether the melanoma has completely destroyed a previous nevus or originated because of cancerization enbloc.—*D. C. Gastineau, M.D.*

Enos, William F., and Holmes, Robert H. Malignant melanoma in the tropics. *Am. J. Path.*, May–June, 1951, *27*, 523–535.

Sixteen cases of malignant melanoma occurring in the Canal Zone are reviewed. Seven of these were in white persons, and 9 were in Negroes, and some

interesting racial differences were observed.

There was a striking variation in the anatomical site of origin between the two races. All of the cases in the Negro occurred on the lower extremity, and all but 1 on the foot. No cases involving the foot occurred in white persons.

In the Negro past fifty years of age the tumor had a strong tendency to remain localized or, at most, extend to the inguinal lymph nodes.

Considerable histopathological detail is given on some of the cases along with illustrations of histological sections.—*G. J. Culver, M.D.*

Melendro, J. Calvo. Infantilismo hidatídico. (Hydatid infantilism.) *Bol. Inst. Pat. Méd.*, May, 1951, *6*, 88–94.

The existence of infantilism in association with hydatid disease was first proved in 1920 by Dévé. The author confirms this opinion. He has observed 15 cases in which infantilism occurred in association with hydatid disease. Five of these cases are described in detail. In these cases, he feels that he has been able to eliminate all other causes for the infantilism and, in each instance, the removal of the echinococcus cyst was followed by normal development. Two of the cases of special interest were identical twins, one of whom acquired hydatid disease and manifested infantilism until the cause of the symptoms was removed.—*M. M. Friedman, M.D.*

Thomsen, Gregers, and Vesterdal, Jørgen. Atypical Hurler's syndrome; a report of 3 cases with a discussion of the differential diagnosis. *Acta radiol.*, May–June, 1951, *35*, 331–344.

Hurler's syndrome was first described by Hurler in 1919 and by Pfaundler in 1920. It has a congenital origin with the following characteristics: moderate dwarfism with abnormal proportions, enlargement of the liver and spleen, corneal opacity, impaired hearing and mental retardation. The head is large with a prominent forehead and a plump face. The hands are claw like. The general appearance of the patient is rather grotesque and accounts for the designation "gargoylism."

Roentgen examination shows a thick-walled skull which is often scaphocephalic or oxycephalic. The sella turcica is large and deep, and there is hypertelorism. There is a kyphosis in the upper lumbar region where the vertebrae are frequently deformed. The bones of the extremities are short and thick with a coarse dense structure. The ribs are broad and club shaped.

The case reports of 3 patients are presented, all of whom had atypical forms of Hurler's syndorme. They lacked corneal opacity and not one of them was a dwarf; only 1 was deaf. On the other hand, all showed splenic and hepatic enlargement, all were grotesque in appearance and all exhibited the roentgenological abnormalities mentioned.—*Mary Frances Vastine, M.D.*

Gillis, Leon, and Lee, Stanley. Cancer as a sequel to war wounds. *J. Bone & Joint Surg.*, May, 1951, *33-B*, 167–179.

In this paper 24 cases are reported in which a squamous carcinoma developed at the site of a war wound. These were selected from a considerably larger number because they allowed no reasonable doubt as to the relationship of the carcinoma to the wound. The authors regard a patient with a chronic discharging sinus or an extensive adherent scar as never safe from the risk of malignant change. Examples are still occurring more than thirty years after the end of World War I. The possibility should be kept in mind by those concerned with the long-term treatment of wounds of this kind. Reasonable prophylactic measures would be excision of adherent or unstable scars with, if necessary, their replacement by suitable pedicle flaps having a good blood supply, and earlier amputation if an osteomyelitic sinus persists for several years and does not yield to treatment. Warty changes or indolent ulceration of scars should be regarded with grave suspicion and investigated by biopsy. Any increase in pain or discharge in association with a sinus should receive prompt attention. Finally, if malignant change supervenes, treatment should be speedy and as radical as with any other cancer.

At least 13 of the authors' patients, 24 in number, have died of cancer.—*R. S. Bromer, M.D.*

Gage, M., and Dawson, W. Malignant melanoma. *Ann. Surg.*, June, 1951, *133*, 772–782.

Malignant melanoma of the skin is a comparatively rare lesion comprising 1.4 per cent of cutaneous malignancies and is associated with high morbidity and mortality. The authors review some of the literature and report five year survival rates varying from zero to 17.7 per cent. In various series of cases recurrence following operation developed in 61 to 80.5 per cent.

The malignant melanoma arises from either a junctional nevus, a compound nevus or a juvenile nevus. The point of differentiation of benign and malignant lesions lies in the degree of cellular activity as arrangement of the abnormal cells is the same in both forms. The juvenile nevus appears maligannt from a histopathologic standpoint but clinically it is benign until after puberty. All these neoplasms metasize by both blood stream and lymph channels and the more anaplastic forms metastasize earlier.

Clinically, increase in size, change in color, inflammation and ulceration indicate malignancy. All pigmented moles located on the palms of the hands, soles of the feet, scrotum or vulva, beneath the finger and toe nails and the eye should be considered as malignant. Melanotic moles subject to constant

trauma by clothing should be considered potentially malignant. Juvenile melanomas should also be considered potentially malignant and should be surgically removed before puberty.

The authors condemn the use of cautery, coagulation, radium or roentgen therapy and inadequate surgery in the treatment of these lesions. Biopsy and use of local anesthetic in simple excision of apparently benign lesions is decried.

Potentially malignant lesions should be removed with a wide segment of normal skin and underlying fascia. Malignant melanomas with no regional lymph node involvement should be treated by wide excision of the primary growth with fascia and lymph node dissection. Patients who have local recurrence or regional lymph node involvement should have as radical a procedure as their condition will permit.—*Robert Emerick, M.D.*

Decker, Alfred M., and Chamness, James T. Melanocarcinoma of the plantar surface of the foot; review of twenty-five cases. *Surgery*, May, 1951, *29*, 731–742.

The authors review 25 cases of melanocarcinoma of the plantar surface of the foot. This represents all cases of primary melanocarcinoma of the sole of the foot that were proved histopathologically at Barnes Hospital, St. Louis, Missouri, and at Ellis Fischer State Cancer Hospital, Columbia, Missouri.

These 25 melanocarcinomas were part of a group of 43 malignant lesions of the sole of the foot found in biopsy of 142 plantar lesions. The other malignant lesions consisted of 10 squamous cell carcinomas, 2 carcinomas of the sweat glands, 1 basal cell carcinoma, 2 liposarcomas, 2 fibrosarcomas and 1 Kaposi sarcoma.

Only 2 patients were less than forty years of age. Ten of the melanocarcinomas were on the metatarsal portion or ball of the foot, and 10 on the heel, the weight-bearing areas thus predominating.

Nine patients had noted the presence of pre-existing moles; in 2 cases moles had existed since the patient's birth and in the other 7 they had been known to exist for from three to twenty years. Of the clinical signs that may have presaged maligant change, the following are mentioned: change from brown to black; growth; pseudopod-like spread of pigment into surrounding skin; daughter lesions close by; ulceration; bleeding; pain. Delay in seeking definitive treatment varied, the longest time being almost nine years. In no case was the correct diagnosis suspected by the physician first consulted by the patient. It is of interest, in this connection, that 8 of the 25 tumors had no pigment grossly, and 6 of the 8 did not contain melanin granules microscopically.

In 9 instances local control was effected primarily and in 6 secondarily. In 10 the local lesion was never controlled and in the majority of these cases the patient survived twelve to twenty-four months. The majority of patients whose local lesions were controlled survived twenty-four to thirty-six months. The authors consider scalpel excision (excision biopsy) preferable to cautery excision. The latter has the disadvantages of possibly activating and spreading the neoplasm, and also of resulting in a slowly healing wound. A margin of at least 3 cm. from the edge of the tumor should be allowed when excising the primary lesion. To put this another way, Pack has recommended that closure of the site of excision of a primary melanocarcinoma on an extremity should require a graft. It is felt, as regards the depth of excision, that excision biopsy should include the entire underlying plantar fascia. Lesions extending deeper than this require amputation.

In 14 of the 25 cases metastasis to the inguinal lymph nodes was clinically apparent and microscopically confirmed. In 8 of the 14 cases the neoplasms were inoperable when the patients were first seen. In 10 cases in which involvement of the inguinal lymph nodes was not evident clinically, prophylactic resection of the inguinal lymph nodes was carried out; microscopic evidence of involved lymph nodes was found in 2 of these cases. In only 1 case was involvement of the popliteal lymph nodes present.

As stated previously, 8 patients had inoperable neoplasms when first seen. None of these survived as long as two years from the time they were first seen by the authors, although 1 had survived ten years and 2 fifteen years from the time of onset. Seventeen were treated by local excision and dissection of the inguinal lymph nodes. Five of these patients were alive without evident recurrence, from six months to six years later. Eleven had died of melanocarcinomatosis after periods varying from four to fifty-five months after dissection of the inguinal lymph nodes. One patient was alive, but with metastasis, fourteen months after treatment.

The authors found benign plantar nevi to be rather rare, and suggested that all nevi on the sole of the foot, whether pigmented or not, be considered malignant until proved otherwise.

It is suggested that lesions 2 cm. or less in diameter (and without deep fixation) be excised en bloc with the plantar fascia including a rim 3 cm. in width of grossly uninvolved tissue, and skin should be grafted. If lesions are larger than 2 cm. in diameter, with deep fixation or with many satellite nodules, the lower portion of the leg should be amputated. All patients without evidence of incurable metastasis should have radical dissection of the inguinal lymph nodes.

Radiation therapy has no place as a primary treatment.—*André Bruwer, M.D.*

## RADIATION THERAPY

Beierwaltes, William H. Irradiation of the pituitary in the treatment of malignant exophthalmos. *J. Clin. Endocrinol.*, May, 1951, *11*, 512–530.

Progressive protrusion of the eyes may occur in

the presence of severe or mild thyrotoxicosis, after successful treatment of this toxic state, or in patients exhibiting no evidence of thyroid disease. The initial symptoms are pain, lacrimation, burning, and less commonly, diplopia. The eyes become proptosed and the lids swell. Exposure keratitis, corneal ulceration, panophthalmitis, surgical loss of the eye, or, rarely, death from meningitis may follow.

The etiology is unknown. Some evidence favors the view that there is hyperfunction of the anterior lobe of the pituitary in a human disease of which exophthalmos is a frequent manifestation.

Treatment of malignant exophthalmos has consisted of local care of the eyes, lowering of the basal metabolic rate when elevated, administration of desiccated thyroid in an attempt to depress the pituitary's output of thyrotropic hormone, and, if these fail, surgical decompression of the orbit.

Review of the literature shows no article written specifically on the use of irradiation of the pituitary for the treatment of malignant exophthalmos.

The author reports on 11 patients with malignant exophthalmos treated by irradiation of the pituitary and followed up to five years. These patients were threatened with immediate loss of vision while under therapy with desiccated thyroid. Exophthalmometric measurements were carried out for an average period of twenty-three months. Roentgentherapy was given using two temporal fields and, in addition, an anterior nasal field in 2 patients. A representative technique was as follows: 200 kv., 25 ma., 50 cm. skin target distance, filtration of 0.5 mm. Cu plus 1 mm. Al, half-value layer of 1.0 mm. Cu, 40 r per minute in air, a daily dose of 150 r in air to each field to a total dose of 700 r per field, with a field size of 8 by 7 cm.

It was found that in patients with malignant exophthalmos a decrease in measurable protrusion of the eyes is rarely, if ever, brought about by lowering the basal metabolic rate when it is elevated, or by administration of desiccated thyroid when it is not. Surgical decompression of the orbit is an effective treatment, but it represents a relatively formidable procedure.

Eight of the 11 patients with malignant exophthalmos had significant regression in exophthalmos, *i.e.*, 2 mm. or more, following roentgen irradiation. Only 1 of the 3 nonresponsive patients showed a significant increase in exophthalmos.

Signs and symptoms of hypopituitarism did not develop. The only side-effects of irradiation observed in follow-ups of as long as three years were transient epilation in all patients, and occasional headaches during the first few weeks after treatment.

The patients who responded showed onset of post-irradiation recession at an average interval of twelve months.

Glaucoma, which was present in 2 of the 11 patients, appears not rarely in association with malignant exophthalmos. It is usually improved by control of the exophthalmos.—*A. W. Finestone, M.D.*

Kelly, Keith H., Feldsted, Eggert T., Brown, Reynold F., Ortega, Paul, Bierman, Howard R., Low-Beer, Bertram V. A., and Shimkin, Michael B. Irradiation of the normal human hypophysis in malignancy: report of three cases receiving 8,100–10,000 r tissue dose to the pituitary gland. *J. Nat. Cancer Inst.*, April, 1951, *11*, 967–984.

The possible role of endocrine influences in malignant melanoma is suggested by the intriguing observations that melanomas in man are rarely malignant before puberty and are not observed in castrated individuals. One speculation is that the action is exerted through alterations in pituitary function. It was therefore decided to attempt reduction of pituitary function in patients by means of irradiation of the pituitary gland.

The authors constructed an apparatus permitting irradiation of the pituitary gland through multiple fields. Measurements were taken on phantom skulls of the exact dosage to the pituitary.

Three patients with far-advanced neoplastic disease were selected for the investigation. All 3 patients had complete clinical studies performed before, during, and after the completion of irradiation to the pituitary gland.

Each patient was given a total of 8,100 to 10,000 r tissue dose to the pituitary gland. No clinical or laboratory evidence of hypopituitary function was noted. The growth of the neoplasm was not affected. Gross and microscopic examination of the pituitary gland and other endocrine organs showed no definite abnormalities in 2 cases coming to autopsy.

It is concluded that the normal adult human pituitary gland is resistant to roentgen irradiation in doses up to 10,000 r.—*V. L. Peterson, M.D.*

Paufique, L., Papillon, J., and Guinet, P. Le traitement roentgenthérapique des exophtalmies oedémateuses sans hyperthyroïdie. (Roentgen therapy of edematous exophthalmos without hyperthyroidism.) *J. de radiol. et d'électrol. & Arch. d'électric. méd.*, 1951, *32*, 21–26.

Pituitary roentgen irradiation has been successfully used in Graves' disease by a number of investigators ever since its introduction in 1925 by Borak, who first applied the method in hyperthyroidism incidental to menopause.

The authors here report their experience with similar treatment in what they believe to be a specific clinical entity characterized by malignant progression of exophthalmos without evidence of hyperthyroidism or any sign of toxicity. Eight patients were treated and their case histories are given in detail.

In studying the etiology of this peculiar entity, the authors found that the following three factors

were significant: (a) in 4 women there was a definite endocrine element, 3 having been operated upon formerly for postmenopausal hyperthyroidism, and the fourth having had Graves' disease since the age of eighteen following psychical amenorrhea; (b) in 6 of the 8 patients the malignant progression of exophthalmos occurred after the hyperthyroidism was brought under control; in 3, moderate exophthalmos was already present prior to the operation but without sign of progression, and in the other 3 it started within two to seven months following thyroidectomy; (c) in all cases, except 1, there was complete lack of thyrotoxicosis.

The exophthalmos usually was bilateral, although at times it progressed more rapidly on one side than the other. It soon led to marked edema of the conjunctiva and eyelids so that the patients could not close their eyes and they developed severe photophobia with constant lacrimation. Five patients were treated at this stage. In 2 others corneal ulcers were already present when irradiation was undertaken. In the eighth patient, who also had Parkinson's disease and marked hypertension at the age of twenty-five, perforation and secondary infection necessitated enucleation of one eye and roentgen therapy was given for progressive exophthalmos of the other.

Roentgen therapy of the pituitary was always associated with medical treatment, consisting of the administration of estrogens, thyroxine, testosterone, etc. The technique of irradiation was as follows: 170 kv., 0.5 mm. Cu, 150–200 r per seance, one to five times per week. In the beginning, only the pituitary proper was exposed but later the orbits were also irradiated. Usually two temporal fields of 5 by 8 cm. were employed including the pituitary and the orbit, to which sometimes an anterior field was added for each orbit. The total doses amounted to from 1,800 to 5,700 r spaced over a period of three to six weeks.

At the present time the authors give single doses of 200 r, repeated three times per week alternatingly over each temporal field until a total dose of 2,000 r per field is reached. The depth dose in the region of the orbital apex amounts to approximately 1,500 r.

A functional amelioration was obtained regularly, consisting of disappearance of the photophobia, regression of the edema and improvement of vision so that patients could resume their activities. The objective benefits, however, were less pronounced. The corneal ulcers healed and the papilledema usually cleared up but the exophthalmos was slow in regressing and it rarely disappeared altogether. The results were somewhat better in the male and in the more recent cases. If the exophthalmos was of more than one year in duration and if the visual acuity was diminished, the response was poor and the unfavorable prognosis could not be altered.

In concluding, the authors express the opinion that roentgen irradiation through a vasomotor mechanism re-establishes the local fluid balance, thereby clearing up the edema and reducing the markedly increased pressure of the intraorbital structures.—*T. Leucutia, M.D.*

Fossati, Franco, and Silvestrini, Franco. La roentgenterapie dell'esoftalmo tireotropico. (Roentgen therapy of thyrotropic exophthalmos.) *Radiol. med.*, Aug., 1951, *37*, 609–621.

The authors discuss in detail the nomenclature used for expressing the various degrees and types of exophthalmos. They give the following definitions: (1) apparent exophthalmos—a protrusion of the eyeball which can be reduced by digital pressure, and which disappears at death or during deep anesthesia; (2) proptosis or real exophthalmos—a protrusion of the eyeball which cannot be reduced by digital pressure and which persists after death or during deep anesthesia; (3) exophthalmic ophthalmoplegia—a disorder of the motor function of the extrinsic muscles (chiefly of the recti) of the eyeball accompanied with exophthalmos; (4) progressive exophthalmos—a proptosis or exophthalmos which may or may not be associated with functional disorders of the thyroid or pituitary glands and which continues to progress despite successful treatment of the basic cause; (5) malignant exophthalmos—this term is used in the same sense as progressive exophthalmos, depicting a rapid clinical evolution with severe conjunctivitis, chemosis, corneal ulcerations and atrophy of the optic nerve, sometimes leading to blindness and necessitating surgical decompression of the orbit or enucleation of the eyeball; (6) intermittent exophthalmos—a variable exophthalmos due mainly to retrobulbar vascular lesions (angioma, aneurysm, varices, etc.); (7) exorbitism—a term used chiefly by the French clinicians to denote dislodgment not only of the eyeball but also of all of the soft tissues of the orbit outside of the orbital cavity.

The authors classify exophthalmos on the basis of pathogenesis and clinical characteristics in the following three groups: (a) thyrotoxic exophthalmos—the type usually observed in Graves' disease; (b) thyroprivic or paradoxical exophthalmos—an exophthalmos which appears following thyroidectomy, as, for example, in Graves' disease, or following chemical block of the thyroid and which probably belongs to the next group: (c) thyrotropic or pituitary-diencephalic exophthalmos—a progressive exophthalmos most probably due to an excess of a pituitary thyrotropic hormone but in which the diencephalic, and especially the hypothalamic nuclei may also have a causative role.

In the present article, the authors are concerned only with thyrotropic exophthalmos. They give a detailed account of the tests used for its experimental identification, describe its clinical features and dis-

cuss its roentgen therapeutic aspect. They also present, in short résumés, the case records of 6 patients who were treated by roentgen therapy.

The technique of irradiation was as follows: 160 kv., 0.5 mm. Cu plus 1 mm. Al, 40 cm. skin-target distance; two temporo-orbital and one frontal field of 6 by 8 cm. each; 150 r (in air) on alternating days to each field until a total dose of 900 r per field was reached. The series sometimes was repeated within one to three months. The lateral fields always included the posterior portion of the orbital cavities but in order to avoid irradiation of the eyeball, and especially of the lens, the tube was slightly tilted toward the occiput. No concomitant hormonal therapy was used in any of the cases, although more recent investigations seem rather encouraging in this respect.

Of the 6 patients irradiated, 2 showed excellent response, 2 were improved and in 2 the treatment remained unsuccessful.—*T. Leucutia, M.D.*

Mallet, L., and Decker, R. La cyclothérapie dans le cancer de l'oesophage; quelques résultats statistiques. (Rotation therapy of cancer of the esophagus; some statistical results.) *Bull. Assoc. franç. l'étude cancer*, 1951, *38*, 308–316.

The authors have used rotation therapy with 190 kv., 18 ma., and 60 cm. anode-skin distance (measured at the sternum), through a field 8 cm. wide and 23 cm. long, for the treatment of 157 patients with cancer of the esophagus. With this method, the tumor dose is 250 per cent of the skin dose. The daily dose given was 150 r (tumor dose), six times weekly, a total tumor dose of 4,500 r being delivered. More recently, three to four series with a tumor dose of 1,500 r were given, interrupted by one week's rest between the series.

Of the 157 patients, 103, or 75 per cent, were referred for radiation treatment as late as three months after the diagnosis had been established; and 46 after at least six months. The authors take a dim view of the "factors of progress," such as esophagoscopy and biopsy, which, in their experience, add nothing to determining the diagnosis that has been previously established clinically and roentgenologically but are often the cause of serious delay of treatment. The great majority of the patients treated by the authors were referred to them after some surgical treatment had been performed. Of those treated with rotation therapy alone (without any kind of surgical therapy), 10 per cent survived for twelve months or longer; of those treated surgically, 7 per cent survived for the same period. Lesions of the cervical part of the esophagus showed the best response; those of the oral and cardiac ends, the poorest. The results also were better in the older than in the younger age groups.

The authors believe that, in the future, treatment of cancer of the esophagus should follow the same rules as treatment of cancer of the uterine cervix; *i.e.*, radiation therapy first, in order to create favorable conditions for surgical intervention.—*Albert Oppenheimer, M.D.*

Holzaepfel, John H. Results of treatment of squamous-cell carcinoma of the cervix. *Cancer*, March, 1951, *4*, 251–254.

The purpose of this paper is to present a series of 225 patients of squamous cell carcinoma of the cervix with 100 per cent follow-up. This was accomplished by consulting the State Bureau of Vital Statistics, local County Health Officers, friends, relatives, and former neighbors.

The Tumor Conference that reviews all gynecological cancers meets once a week and is composed of clinicians, radiologists, and a pathologist. The patients are classified and treatment recommended by the Conference. Re-examination during therapy and adaptation of the therapy schedule to each patient is also accomplished through the Conference. The Conference secretary is assigned the task of maintaining therapeutic schedules because of voluntary lapses of treatment in a few patients who do not appreciate the hazardous nature of the disease.

The cases were reviewed and only 17 patients previously treated were classed as "therapy not acceptable." These are summarized in a table. There were 26 cases with reported morbidity and these are tabulated separately. All of the cases treated, including the ones with previous "therapy not acceptable" as well as the cases of morbidity, are listed in the survival table. The total five year survival rate was 28 per cent.

Therapy can only be evaluated by an adequate follow-up. The authors believe that the percentage of five year survivals will be increased appreciably as all patients are given tolerance treatment. The paper presents the statistical analysis of absolute survival with all cases reporting to the Conference included in the analysis.—*D. C. Gastineau, M.D.*

Prossor, T. M. Malignant disease of the testis; with special reference to radiotherapy. *Brit. J. Surg.*, April, 1951, *38*, 473–481.

As the author states, the object of this article is to discuss some of the facts associated with malignant disease of the testis, with special reference to the place of radiation therapy in its treatment.

He classifies tumors of testis into three groups:

1. Seminoma—which was the most common, comprising 84 of 147 cases.
2. Teratoma—of which there were 61 cases.
3. Chorionepithelioma—of which there were only 2 cases.

Histogenetically the teratoma is considered to be a tumor arising from pluripotential embryonic cells. It is believed that, during early development,

these cells have escaped the influence of the morphogenic hormones known as organizers, which are chemical substances of the nature of sterols, controlling orderly development. This theory is based on the work of Needham (1936). As regards seminoma, Chevassu (1906) expressed the opinion that it is a carcinoma of the epithelium of the seminal tubules, but in 1911 Ewing maintained that it represents one-sided development of a teratoma. Harvey, Dawson and Innes (1940) held that the two views can be reconciled by assuming that both seminoma and teratoma are derived from totipotent cells in the germinal epithelium. The chorionepithelioma is considered to have the same origin as teratoma.

A chapter on morbid anatomy and histology is given. The author states that the cardinal features of a teratoma are its great complexity and the fact that structures derived from all three germinal layers are found in it. In marked contrast, the seminoma contains evenly distributed large or medium sized spheroidal or polyhedral cells with distinct outlines, clear pale cytoplasm, and round hyperchromatic nuclei. The cells, which at times resemble spermatocytes, are disposed in sheets or bands. The chorionepithelioma is usually a small tumor, soft and very liable to necrosis and hemorrhage. Its structure consists of masses of irregular multinucleated undifferentiated epithelial cells with a substrate of large, clearly defined polygonal or round cells having single nuclei—the so-called Langhans cells.

The peak incidence in the reported series was observed between 20–30 years in teratoma and 30–40 years in seminoma. The youngest patient was nineteen and the oldest fifty-eight years of age. Undescended testes were found in 6 per cent of the cases.

Gradually increasing, sometimes painful, testicular enlargement was the commonest and earliest symptom. When the diagnosis is doubtful, excision of the diseased organ is advisable. The Aschheim-Zondek and Friedman tests are not always reliable.

In the author's series the incidence of metastases was 54 per cent in teratoma, whereas in seminoma it was only 35 per cent. The over-all incidence was 50 per cent (74 of the 147 cases); 44 patients had metastases when first seen and in 30 they developed later. The most commonly involved structures were the para-aortic and iliac lymph nodes (53 per cent), followed in decreasing order by the lungs, the supraclavicular lymph nodes, scrotum and inguinal lymph nodes, mediastinum, liver, bones, and kidneys.

In prescribing treatment, a knowledge of the distribution of the lymphatics is of paramount importance. This is discussed and demonstrated by a drawing. The author feels that radical excision of the lymph nodes is not indicated because of the difficulty in dissection and the chance of spreading the disease.

The majority of the cases were treated with 220 kv., 20 ma., half-value layer of 2.2 mm. of copper and a focal skin distance of 50 cm. The lower para-aortic and iliac lymph nodes were irradiated first through two opposing 20 by 20 cm. fields, a total dose of 2,500 to 3,000 r being delivered in thirty days. Six weeks later the upper para-aortic lymph nodes were irradiated through two opposing 15 by 10 cm. fields.

The cases with spread to the supraclavicular fossa or inguinal lymph nodes were treated with the 4 gram teleradium unit. The teleradium technique was also used in 12 of the earlier cases for abdominal metastases either alone or in combination with roentgen therapy. Examples are presented showing the results of treating recurrences over a period of years with the various techniques.

The results in the 147 patients are given. The series is divided into two groups: 1—those patients without any clinical evidence of metastases (103 cases); 2—those with metastases (44 cases). In the first group 57 patients were seen before 1945: 48 with seminoma and 9 with teratoma. The five year survival rates were 66 per cent and 55 per cent respectively. In the second group there were 10 patients with seminoma, 10 with teratoma, and 13 without histopathological confirmation. Here a five year survival rate of only 15 per cent was obtained.—*L. L. Lemak, M.D.*

Kepp, R. K. Zur Frage der strahlentherapeutischen Anwendung schneller Elektronen. (The question of the radiotherapeutic use of fast electrons.) *Deutsche med. Wchnschr.*, May 11, 1951, *76*, 639–644.

In discussing the principle of the betatron (or the Elektronenschleuder—electron sling—as it is called in German), the author calls attention to the 6 and the 15 mev. apparatus built by Siemens-Reiniger in Erlangen. These betatrons can be used to produce either fast electron beams or supervoltage roentgen rays. The importance of the number and the spatial distribution of ions formed by any type of radiation in correlation with the biologic effect produced is described. Terms such as specific ionization density or differential ionization, medium ionization density are discussed in detail. Fast electrons are characterized by having a considerably smaller medium ionization density than roentgen rays. Irradiation of human tissue with fast electrons will therefore be less effective for equal doses than with roentgen rays. On the other hand, a radiation with low ionization density will produce greater biologic effects if it is applied in large doses.

In contrast to the absorption of roentgen rays, the electrons are quickly stopped in tissue and their ionizing path is relatively short. For a 6 mev. betatron the range of the electron beam is about 3 cm. The spatial distribution of the electrons in tissue depends upon the ratio between diameter of the irradi-

ated area and the range. If the area has a diameter of the order of length of the range, there is an increase of dose beneath the surface with a maximum within about 30 per cent of the range of the electron beam. This maximum increases with greater energies of the beam. One can therefore arrange to have a maximum dose at a chosen depth together with a rapid drop of the dose beyond that point. Actual studies of irradiation with electron beams on patients have shown that the healthy tissue is apparently more resistant to the electrons than tumor tissue and that this difference seems to be more pronounced for protracted dose applications. Treatment of superficial skin tumors, recurrent skin breast tumors, lymph node metastases, and carcinoma of the vulva with the 6 mev. betatron at the Physical Institute of the University of Göttingen is described. Results have been very satisfactory. The same results on superficially located tumors can be obtained with current methods of irradiation but the author feels that experience gained with relatively low energy betatrons will be very useful when higher energy betatrons with deeper penetrating electron beams become generally available. Then it will be possible to evaluate the limits of each method.—*Otto Glasser, Ph.D.*

Garland, L. H., Hill, H. A., Mottram, M. E., and Sisson, M. A. Nasopharyngeal irradiation; relative merits of roentgen and radium therapy for benign conditions. *J.A.M.A.*, June, 1951, *146*, 454–460.

Hyperplasia of the lymphoid tissue of the nasopharynx has been treated with irradiation. A review of the literature shows good results with both radium and roentgen treatment. This article gives tables showing depth dosages and distribution of radiation using the usual type of radium applicators, and roentgen irradiation.

With radium a very high dose is delivered to a small area about the applicator with a rapid fall 30 mm. from the applicator.

With roentgen radiation a uniform dose can be given to the whole nasopharynx. There is some danger of ulceration from the radium applicator which is not present when roentgen rays are used.

The results of treatment with roentgen rays are as good as with radium in treating deafness due to hypertrophy of the lymphoid tissue about the eustachian tube, and it has the advantage that lymphoid tissue elsewhere in the nasopharynx is destroyed.—*F. H. Squire, M.D.*

Costolow, William E. Radiation therapy in diseases of the genito-urinary tract. *Urol. & Cutan. Rev.*, June, 1951, *55*, 324–327.

This article is a brief and generalized summary of diseases of the male genitourinary tract and of tumors of the kidney and bladder treated by irradiation.

In the series of 32 patients with Peyronie's disease, 18 were improved and 10 had a clinical cure following the topical application of radium to the areas of the fibrosis in the corpora cavernosa. The author points out that both surgery and irradiation have been employed in this disease but the results in general have not been completely satisfactory.

The treatment of carcinoma of the penis may be by irradiation or surgery. Irradiation, preferably in the form of radium application, is used for a smaller lesion, 1 to 2 cm. in diameter, and when there is no evidence of metastasis. The dose is fractionated so as to secure adequate tissue effect with minimum skin reaction. In the larger lesions or in those which do not respond to radium therapy, surgery is required. The inguinal metastases of primary carcinoma of the penis are best treated by surgery although the results of dissection of the lymph nodes are not entirely satisfactory. External roentgen therapy in this region is of no practical value.

For the treatment of tumors of the testis, orchiectomy followed by thorough roentgen irradiation of the areas of lymphatic distribution is recommended. Seminoma and embryonal carcinoma are radiosensitive and give the best results whereas chorionepithelioma shows a very poor prognosis. Some teratomas should be treated but the adult teratomas are radioresistant. In the author's series of 50 cases, there was a survival rate of 47 per cent in 23 cases of seminoma. The over-all five year survival rate for the tumors of the testis was 36 per cent; 56 per cent of this group had metastases when first seen; 33 per cent of those with metastases survived five years.

It is well agreed that in carcinoma of the prostate, early radical removal is the only method offering a cure. All other methods of treatment are palliative. Radiation therapy has produced very little benefit in primary carcinoma of the prostate. It may be used in the metastatic bone lesions with some success as a palliative procedure, particularly in conjunction with hormone therapy and castration.

In the group of kidney tumors, radiation therapy is most valuable in Wilms' tumor. This tumor is radiosensitive and a combination of preoperative irradiation and surgery is often recommended, although the ultimate results are consistently poor. The metastases from Wilms' tumor are likewise radiosensitive.

Radiation therapy pre- and postoperatively may also be given to renal carcinoma in selected cases.

Treatment of bladder carcinoma may be by (1) fulguration; (2) irradiation; (3) surgical resection of the local growth; (4) radical cystectomy. Combinations of several of these methods may be used, especially a combination of fulguration and irradiation. Radiation therapy may be given externally or in the form of radon seeds or low intensity platinum needles. Probably the best results are obtained in those patients who have papillary growths within the

bladder. The prognosis of infiltrating carcinoma of the bladder is very poor and if the lesion has extended outside the bladder, the prognosis is hopeless. In the author's series of 24 cases of carcinoma of the papillary type, there was a 33 per cent five year survival. In 33 cases of carcinoma of the infiltrating type, the five year survival rate was 6 per cent.—*G. W. Chamberlin, M.D.*

Kistner, Robert W., and Hertig, Arthur T. A correlation of histologic grade, clinical stage, and radiation response in carcinoma of the uterine cervix. *Am. J. Obst. & Gynec.*, June, 1951, *61*, 1293–1300.

In an attempt to correlate histopathologic grade, clinical stage and radiation response, the authors gathered 100 cases in which pre- and post-irradiation biopsies were available at the Free Hospital for Women, Brookline, and the Harvard Medical School. Previous studies of histopathologic grade and survival showed little correlation between the two, even though local tissue response corresponded fairly well with the law of Bergonié and Tribondeau.

The tumors were graded microscopically according to the method of Warren into Grades I, II, III and adenocarcinoma. The clinical staging followed the classification of the League of Nations. The radiation response observed in the tumor cells was graded as marked, moderate and minimal.

The over-all five year survival rate was 50 per cent with good correlation between clinical stage and survival: Stage I, 74 per cent; Stage II, 46 per cent; Stage III, 12 per cent; Stage IV, 0 per cent. No clear relationship existed between histopathologic grade and survival rate. Those cases which showed a marked reaction to irradiation also showed an increase in survival rate, but when these cases were analyzed according to stage, the latter affected the survival rate more decisively than did the degree of local tissue response.

The authors conclude that the major factor in the survival rate of patients with carcinoma of the cervix is the clinical stage of the disease and that radiation response, as evidenced by post-irradiation biopsy, is of less importance. Surgery is advised as adjunctive treatment, where radiation response is minimal.—*H. J. Klos, M.D.*

Pierquin, Jean, Richard, Georges, and Pierquin, Bernard. La radiothérapie dans le traitement de l'angiomatose hémorragique familiale; maladie de Rendu-Osler. (Radiotherapy in the treatment of hemorrhagic familial angiomatosis; Rendu-Osler's disease. *Presse méd.*, May 23, 1951, *59*, 733–734.

After a brief summary of the essential characteristics of Rendu-Osler's disease, the authors state that the fragile blood vessels of the lesions are formed of young endothelial cells which are radiosensitive.

For the treatment of epistaxis they recommend a tandem of 3 radium capsules, each capsule containing 5.5 mg. of radium filtered by 1.0 mm. of platinum, to be placed in the nasal cavity for twenty-four hours on each side, the total dose being 6 mcd. A larger dose may cause perforation. Cutaneous lesions of the face may be treated by 120 kv. radiation, the dose being 500 r per treatment repeated at intervals of three weeks for a total dose of 1,500 r. In all 9 cases treated by radium in the past year and a half, epistaxis was stopped immediately and did not recur during this brief period of observation.

Superficial roentgen therapy applied to the face in 5 of these cases produced a slow but equally efficacious regression of the cutaneous lesions.—*S. M. Silverstone, M.D.*

## RADIOISOTOPES

Aufranc, W. H. Mobilization of health resources for defense. *Radiology*, May, 1951, *56*, 641–644.

The work being carried out by the Health Resources Office of the National Security Resources Board and the Health Resources Advisory Committee is summarized. The former is carrying out surveys on a county, state, and nationwide basis of the minimum requirements for medical personnel and medical supplies while the latter uses the above information to advise the Department of Defense and Selective Service in the procurement of medical personnel and supplies.—*M. B. Goodwin, M.D.*

DeCoursey, Elbert. Injury from atomic bombs. *Radiology*, May, 1951, *56*, 645–652.

Effects of air detonation of a Nagasaki type atomic bomb at approximately 2,000 feet above the ground are discussed. Human injury is caused by the air blast, thermal radiations, and ionizing radiations. The air blast differs from that of a TNT bomb in that the pressure change is slower, practically never causing direct sublethal injury such as ruptured ear drums and internal hemorrhage. Injury is caused indirectly by flying debris and falling buildings, the destructive radius being approximately 2 miles. Reinforced concrete walls without plaster and deep hollows provide protection.

The thermal radiation, mixed with a small amount of ultraviolet radiation, is unidirectional, travels at the speed of light, probably lasts less than three seconds, and has an effective radius of $2\frac{1}{4}$ miles. A thin layer of light clothing will tend to protect the exposed surface of the body, thin blades of grass casting shadows on charred wood. The severity of flame burns, resultant of fires caused by blast destruction bears no relation to ground zero. These secondary fires tend to be drawn to the center of the blast

area by the rising atomic cloud. Probably 50 per cent of deaths are caused by burns.

Gamma rays originating from fission products in the fire ball are the main source of radiation injury. Neutrons and alpha and beta particles seldom reach the earth from 2,000 feet and the fire ball rises at an average rate of 10,000 feet per minute following detonation. Residual radiations from "fall out" of fission particles is of academic interest only. Fifteen per cent of the gamma-ray dosage is delivered in 0.1 second, 50 per cent in 1 second, and 80 per cent in 10 seconds. Total dosage is less than 1 r at a distance of 2 miles, 400–500 r at 4,000 feet, and 10,000 r at ground zero. Twenty inches of earth, 12 inches of concrete, 4 inches of iron, or 2 inches of lead would reduce the dosage to below 400 r at a distance of 2,250 feet.

The injury due to radiation is well summarized. It may be first evidenced clinically by nausea and vomiting on the day of the bombing, or by striking leukopenia. Epilation and purpura may become prominent after the second week. Pathologically the bone marrow, lymphoid organs, intestinal tract, gonads, and hair follicles show definite lesions, breakdown of the reticuloendothelial system being paramount. Patients are easily divided into groups presenting clinical, pathologic, mortality, and distance correlations. Ionizing radiation produces 12–25 per cent of the casualties.

Within 2,000 feet, the effects of either the air blast or thermal or nuclear radiations are considered lethal. Lifesaving evasive action is possible even after the flash of the detonation has been seen because only 50 per cent of the gamma radiation and possibly only part of the thermal radiation is received in the first second.—*M. B. Goodwin, M.D.*

Harvey, Roger A. Preliminary suggestions for additional teaching in radiological aspects of atomic defense. *Radiology*, May, 1951, *56*, 653–655.

Undergraduate medical students should have a basic understanding of atomic medicine. Lectures covering the following are recommended:

1. The physics and mechanical effect of atomic explosions.
2. Self protection from atomic radiations.
3. Decontamination.
4. The pathology of radiation damage.
5. Altered susceptibility from radiation injury.
6. Detection of radiation hazards.
7. Clinical findings and therapy.
8. Devices for protection.

Extra teaching by the various departments totalling thirty-six hours is advised. Sources of material are listed.—*M. B. Goodwin, M.D.*

Bale, William F. The detection of radiation hazards; instruments and personnel. *Radiology*, May, 1951, *56*, 656–660.

Instruments for the detection of relatively high energy contamination following an atomic blast are discussed. The fact that an air detonation is likely to leave no dangerous contamination suggests the need for a personal detector of low cost to give assurance to the individual. The glass bead apparatus of Failla is one such device.

But it is possible that an area may become contaminated, making it necessary to have survey instruments available. An instrument for the measurement of intensity of gamma rays should be fool proof, easy to read, have a range from a few milliroentgens to 600 roentgens per hour, and be low in cost. An ideal instrument has not yet been devised. Beta rays have little penetrating power but may injure hands and feet during rescue operations. A satisfactory device for measuring the intensity of beta rays in roentgen equivalent physical is not available at present.

It is probable that 200,000 disintegrations per minute of beta-gamma activity can be well tolerated in drinking water for ten days. Such a limit is well within the range of a Geiger-Müller counter registration. These instruments are readily available and are easily calibrated for the purpose.

Personnel dosimeters for casualty segregation purposes and for disaster relief workers are reviewed. These devices measure the total radiation received by the individual rather than the intensity of radiation at any given time. A great many methods are under consideration but the ideal device has yet to be developed.—*M. B. Goodwin, M.D.*

Cronkite, Eugene P. The diagnosis, prognosis, and treatment of radiation injuries produced by atomic bombs. *Radiology*, May, 1951, *56*, 661–669.

The greatest hazard in atomic warfare is panic caused by the overwhelming fear. Although radiation injury may be responsible for only 10 per cent of the casualties in an atomic blast, this may still include a large number of people.

In regard to prognosis, the author divides those injured with radiation into three groups.

Group I (Supralethal Doses). If vomiting occurs on the day of the bombing and is followed by diarrhea, prostration, continued vomiting, anorexia and fever, survival is improbable, and death will occur in a matter of days.

Group II (Lethal Range). If vomiting occurs on the day of bombing and is followed by an asymptomatic period of one to three weeks before appearance of the typical symptoms of radiation injury (purpura, epilation, ulcerations of the mucous membranes, and gastrointestinal disturbances), survival is possible.

Group III (Sublethal Radiation Injury). If there is no vomiting on the day of the bombing, survival is probable unless there are complicating factors

such as burns, thermal injuries, traumatic injuries, or concomitant epidemics.

There is no effective treatment for Group I. The major therapeutic problem is the treatment of Group II casualties. Four lethal factors in Group II are (1) infection, (2) hemorrhage, (3) anemia and, (4) electrolyte disturbances. The management of these factors is discussed. Group III casualties per se will represent the same therapeutic problems as Group II, but on a lesser scale. This group and the survivors of Group II will constitute the major long term problems so far as study of the population for latent effects (cataracts, leukemia, cancer, etc.) is concerned.—*E. E. Seedorf, M.D.*

Schwob, Claude R. Radioactive decontamination. *Radiology*, May, 1951, *56*, 670–674.

Underwater, underground, and surface bursts of an atomic bomb will cause widespread contamination which may cover 4 square miles or more. An air blast will cause relatively little contamination.

There will be more contamination on horizontal surfaces than on vertical ones.

There will be more contamination on rough, porous surfaces than on smooth, hard ones.

The greater the amount of contamination on a given surface, the greater the fraction that will be readily removed by simple means.

Time is very important in decontamination. In the interval after the burst, the radiation decays rapidly. Decontamination, at best, consists in the transfer of radioactive material from an undesirable location to another where it can be tolerated. There is no neutralization of radioactivity.

Various methods of removing the radioactive contaminated surface of objects are described. Contaminated clothing should also be discarded. Food which is tightly sealed should not become contaminated. The water supply is discussed, but since there is an abundance of water, an uncontaminated supply will probably be available.—*E. E. Seedorf, M.D.*

Behrens, C. F. Evaluation of radiologic hazards and therapy of radiation illness. *Radiology*, May, 1951, *56*, 675–683.

The permissible limit of radiation of 0.3 r per week devised to take care of customary working risks over long periods of time is not applicable to wartime radiation hazards.

The author considers 25 r as the ordinary limit of rapidly accumulative dosage within which no trouble need be anticipated. He considers the 50 r zone as a level at which few people are likely to have minor symptoms and 100 r as the zone at which grave concern should begin. The 200 r zone means serious radiation illness to all concerned, and occasional fatalities. Acute dosages over 200 r involve rapid onset of incapacity and increasing mortality.

The necessity of educating the public to a wholesome respect for the actual hazards and preventing the imagination from running riot is stressed.

Delayed acute effects tend to occur in the second week. Some effects relate to malaise, lassitude, gastrointestinal symptoms, low blood counts, diarrhea, hemorrhages, anemia, and infection.

Remote effects are discussed in relation to carcinogenic effect, general health, impotence, sterility and genetic influence.

Compensatory time away from radiation exposures is dependent upon the amount and rate of exposure.

The section of dosimetry considers film badges, pocket dosimeters, and crystal dosimeters for detection of radiation in a given locality.

Therapy of radiation illness is fully described under the headings of (1) Prophylactic Agents, (2) Specific Medication, and (3) General Measures, all of which are also in general use following conventional radiation therapy.—*E. E. Seedorf, M.D.*

Reiss, M., Hemphill, R. E., Maggs, R., Smith, S., Haigh, C. P., and Reiss, J. M. Thyroid activity in mental patients; evaluation by radioactive tracer methods. *Brit. M. J.*, May, 1951, *1*, 1181–1183.

The authors have studied the thyroid in a group of 541 psychiatric patients by means of the radioactive tracer method. They feel that this method is capable of detecting slight degrees of disturbance of the thyroid activity with a precision heretofore not obtainable.

It has been found that in more than 50 per cent of male anxiety patients, the thyroid activity was subnormal. In female anxiety patients, thyroid function was usually above normal, and in acute female schizophrenia patients, thyroid function was usually increased.

The authors point out the possibility that there may be a correlation between brain metabolism and thyroid function, and they encourage further study along the lines of prolonged thyroid medication in certain psychotic disorders.—*C. L. Hinkel, M.D.*

Allen, H. C., Jr., Libby, R. L., and Cassen, B. The scintillation counter in clinical studies of human thyroid physiology using $I^{131}$. *J. Clin. Endocrinol.*, May, 1951, *11*, 492–511.

The use of directional wide angle scintillation counters combined with eight day iodine ($I^{131}$) in doses of 10 microcuries to study human thyroid physiology has been the purpose of the authors' study as presented. Scintillation counters of the type used were found to be far more efficient detectors of the gamma radiation than the most sensitive of the present Geiger-Müller tube counters.

It has consistently been a problem in the use of $I^{131}$ for therapy to determine the amount of radiation delivered to the thyroid. Any calculation of total

irradiation involves a knowledge of the total weight of the gland, the total amount of radioiodine present in the gland, its distribution within the gland and its biologic half-life. Since the total amount of radioiodine present and the biologic half-life can be measured, the authors have made an approach to the other problems. They have also made an attempt at use of relatively harmless, small tracer doses.

The authors' approach to the above problems has involved the employment of two types of scintillation counters. The first type is a directional scintillation gamma-ray detector designed principally for the delineation of areas of radioactivity, whereas the second is a wide angle scintillation gamma-ray detector designed for thyroid uptake studies utilizing small tracer doses of $I^{131}$.

By comparative studies the authors determined that their directional scintillation counters had a sensitivity of 15 and 27 times greater per area unit as compared to a conventional end-window Geiger tube. The wide angle scintillation counter had a sensitivity of about 94 times that of a Geiger-Müller tube, hence permitting doses of only 1 to 10 microcuries of $I^{131}$ to be used for tracer studies in thyroid physiology.

The authors present rather detailed descriptions and diagrams of the scintillation counters and accessory equipment they used, as well as a discussion of their operational set-up for *in vivo* measurements.

A description is given of a method of delineation of thyroid shape and size using the directional scintillation counter and various doses of $I^{131}$. The method consists essentially of placing a plastic shield over the neck region above which is placed a cellophane sheet which is marked with coordinate guide lines forming $\frac{1}{4}$ inch squares. Multiple point readings with the directional scintillation counter are then made and the points charted to give a relative outline. The *in vivo* studies were checked against operative and autopsy specimens revealing a rather high degree of accuracy in these studies.

The second portion of the article deals with the use of the wide angle scintillation counter in $I^{131}$ uptake studies using tracer doses of 10 to 20 microcuries. The authors have provided charts to illustrate the uptake in hypothyroid, euthyroid, and hyperthyroid subjects.—*J. M. Monaghan, M.D.*

McCullagh, E. Perry. Results of nonsurgical treatment of hyperthyroidism. *Cleveland Clin. Quart.*, April, 1951, *18*, 102–116.

This is a comprehensive survey of the three main methods of treatment of non-malignant disease of the thyroid gland.

The author compares the results of surgical removal with those of antithyroid drugs and radioactive iodine therapy. He agrees that in discrete adenomas surgical removal is the best treatment. In diffuse toxic goiter he feels that radioactive iodine therapy will produce the most satisfactory results unless the patient is so toxic that speed in treatment is important. He feels particularly that in elderly patients radioactive iodine therapy is the method of choice. The initial dose of radioactive iodine depends upon the estimated size of the gland and the basal metabolic rate. For a gland estimated at 30 gm. with a basal metabolic rate above plus 50 per cent the initial dose is 6 millicuries of radioactive iodine ($I^{131}$). With a gland estimated at 120 gm. and the basal metabolic rate above plus 50 per cent the estimated dose of radioactive iodine is 16 millicuries. The results of radioactive iodine therapy in over 200 patients show about 15 per cent hypothyroidism and a recurrent rate of about 2 per cent.

This is a comprehensive article which should be read in its entirety by anyone interested in the treatment of thyroid disorders.—*R. P. Barden, M.D.*

Ashkenazy, Moses, Davis, Loyal, and Martin, John. An evaluation of the technic and results of the radioactive di-iodo-fluorescein test for the localization of intracranial lesions. *J. Neurosurg.*, May, 1951, *8*, 300–314.

Radioactive di-iodo-fluorescein was used in the study of 340 patients with the diagnosis of a space-occupying lesion of the central nervous system. The findings were correlated with the preoperative clinical diagnosis, electroencephalography, pneumography, angiography and with surgical and autopsy findings. There were only 17 proved inaccuracies, making a total accuracy of 95 per cent for the radioactive di-iodo-fluorescein test. The negative findings with this test were also 95 per cent accurate. Localization with di-iodo-fluorescein was much more precise than with electroencephalography or pneumography, whenever verification was obtained at surgery or at autopsy.

After the intravenous injection of a measured amount of radioactive di-iodo-fluorescein, the radioactivity is counted and recorded mechanically. The various sites on the skull have a normal range of radiodye concentrations at specific time intervals and for specific areas of the brain. At least 10–20 normal patients without tumors should be plotted in order to standardize these areas.

Ideally the best results would be obtained if symmetrical areas were recorded at the same time. This is not possible with present equipment; therefore, readings are made on both sides within three to five minutes. The readings are recorded at each site for three minutes. All 32 sites should be counted within a two hour interval since after this the differential concentrations are no longer striking. If differences of over 40–50 counts per minute are found at any 2 symmetrical sites these should be checked immediately. Suspected areas should be counted 2 or 3 times and reference made to the proposed normal chart. In certain acellular, avascular, or hypoplastic

organic lesions such as an astrocytoma, a calcified oligodendroglioma or a cystic or necrotic lesion the differences are only between 40 to 90 counts per minute. If the lesion is highly anaplastic, very cellular or has proliferative new blood vessel formation, the resultant increased permeability causes such high concentrations of radioactive dye that the readings are definitely pertinent because of their heights, 80 to 200 counts per minute. They persist up to four hours following the intravenous administration of the dye. This is particularly true in the highly cellular meningiomas, glioblastomas, carcinomas and sarcomas, if they do not show marked cystic or necrotic changes.

Special positions are necessary in order to locate certain deep-seated and midline lesions. In such cases symmetrical readings, though high, will be equal. Sites on the malar bone, the external auditory meatus, the mastoid and the external occipital protuberance are all of value.

Differences in the state of the capillary endothelium determine the selective deposition of the radiodye within the tumor tissue. The radiodye concentrations are directly proportional to the angioarchitectural histopathological patterns. Changes in the endothelial permeability permit the exudation of foreign substances such as vital dyes. It is possible that the increased cellularity of a tumor may also be responsible for the increased uptake of the radiodye.

The authors believe that the degree of vascularity of a lesion is a major factor since the highest radiofluorescein concentrations occur within the first hour after the administration of the dye. They believe that the endothelium of the terminal capillaries is of the greater importance and not the larger blood vessels. Intracranial aneurysms give relatively normal radiodye findings. The more vascular and more cellular tumors exhibit higher radioactivity than the relatively avascular and acellular ones.

If the observations in a brain tumor suspect show 100 to 600 counts per minute more than the highest recorded normal count at the particular time interval, then pathological endothelial permeability must exist. If cerebral trauma is suspected a recheck study performed in ten to fourteen days will show a decreased radiodye concentration. If the radiodye concentration still remains high or becomes even higher, the presence of a progressive vascular endothelial lesion such as observed secondary to changes in an anaplastic neoplasm is probable.

The radiodye test does not differentiate an acute infection from an anaplastic tumor. However, if the infection has gone beyond the stage of "cellulitis" and a well encapsulated abscess develops with no deranged blood vessels for the radiodye to escape from, normal concentrations result. The same explanation is pertinent in differentiating an acute intracranial hemorrhage from a chronic subdural or intracerebral hematoma. In a cystic degenerative tumor, only the actively growing tumor tissue concentrates the dye.

There were no major untoward reactions. The highest concentration of the radioactive di-iodofluorescein after the initial maximum occurs in the thyroid gland and the dose of radiation delivered to it is about 8 equivalent roentgens. This dose is less than that received by patients tested with radioiodine in studies of the thyroid function.

There are no contraindications to the radiodye test with regard to age, arteriosclerosis, thrombotic episodes, acute intracranial hemorrhage, hypertension, or cardiac decompensation. This test gives better results in the presence of increased intracranial pressure, since the vascular permeability changes are greater.—*F. J. Rigos, M.D.*

Adams, John E. Tracer studies with radioactive phosphorus ($P^{32}$) on the absorption of cerebrospinal fluid and the problem of hydrocephalus. *J. Neurosurg.*, May, 1951, *8*, 279–288.

The author studied the uptake of radioactive phosphorus ($P^{32}$) in the superior longitudinal sinus following its introduction into the ventricular system in dogs, in humans with normal cerebrospinal fluid dynamics, and in 6 hydrocephalic infants. Several patients who were undergoing a prefrontal lobotomy, with presumably normal absorptive processes, had two burr holes made over the superior longitudinal sinus, one anteriorly and one posteriorly. In 5 of these patients the anterior burr hole was just posterior to a point where one or more communicating veins from the surface of the cortex entered a pacchionian granulation. These vessels were tied. Samples of blood were obtained from the superior longitudinal sinus from both burr holes and the effect of such ligation studied.

Consistent measurements were obtained for the rate of uptake of the tracer in the superior longitudinal sinus, its disappearance from the ventricular system and the amount of urinary excretion of the tracer for the first twenty-four hours following its injection.

It appears that the main absorptive bed for cerebrospinal fluid is not in the arachnoidal villi of the pacchionian granulations, but lies distal to this point and is presumably in the capillaries and possibly the small veins of the pia-arachnoid.

A decreased rate of uptake into the superior longitudinal sinus, a decreased rate of disappearance from the ventricles, and a decreased twenty-four hour urinary excretion was found in 4 hydrocephalic infants. Two hydrocephalic infants had entirely normal valves and it is questioned as to whether this represented an overproduction of fluid as a cause of the hydrocephalus.—*F. J. Rigos, M.D.*

Odell, Richard T., Mueller, C. Barber, and Key, J. Albert. Effect on bone grafts of radio-active isotopes of phosphorus. *J. Bone & Joint Surg.*, April, 1951, *33-A*, 324–332.

The purpose of this investigation was to determine the variations in the uptake of radioactive phosphorus ($P^{32}$) by autogenous bone and various types of preserved bone both when utilized as inlay grafts and when placed intramuscularly.

Fourteen dogs were used to measure the relative rates of phosphorus-ion exchange from autogenous, boiled, frozen, and merthiolate bank bone. Comparing the rate of uptake of $P^{32}$ by boiled and frozen inlay grafts in the tibia to that of autogenous inlay grafts at one, two, three and four weeks, three days after subcutaneous injection of radioactive phosphorus, the authors showed that autogenous bone becomes more radioactive than the other varieties. The same was found to be true for autogenous, boiled, frozen, and methiolate bone when placed intramuscularly for two, three and four weeks.

The authors do not believe that this is evidence of the validity of autogenous bone as compared to types of preserved bone. Neither do they feel that this is proof that all free grafts are dead. It corroborates their clinical impression that autogenous bone best serves the purpose of a free graft. They feel that the increased uptake of $P^{32}$ by autogenous over other types of free grafts indicates that the recesses of these grafts are more easily reached by the perfusing solutions, due perhaps to the lesser alteration of the protein matrix.

They conclude that analyses of autogenous, boiled and frozen grafts show no significant alteration in the content of total inorganic phosphorus in bone with time or condition of the graft. The uptake of radioactive phosphorus by inlay autogenous bone grafts is more rapid than the uptake by similar grafts of boiled or frozen bone. The uptake of radioactive phosphorus by intramuscular autogenous bone chips is more rapid than the uptake by frozen or boiled bone. Merthiolate bone consistently takes up less radioactivity than boiled or frozen bone.—*R. S. Bromer, M.D.*

Morton, Joseph L., Callendine, George W., Jr., and Myers, Wm. G. Radioactive cobalt$^{60}$ in plastic tubing for interstitial radiation therapy. *Radiology*, April, 1951, *56*, 553–560.

A method is outlined whereby cobalt 60 (half life 1,940 days, gamma-ray energy 1.16 and 1.31 mev., beta-ray energy 0.31 mev. max.) may be used to supplant radium needles. Cobalt alloys have many practical advantages over radium, one being their low energy beta radiation, 93 per cent of which may be filtered out by a thickness of 0.25 mm. of nylon. Nylon tubing, 1.27 mm. outside diameter, may be loaded with sections of radioactive cobalt wire such that a flexible tube of any given length has an initial linear intensity of approximately 1 millicurie per cm. Aluminum spacers may be used to decrease this intensity if desired. Full details of sources, loading, and sterilization are given.

The flexibility and adjustable intensity per linear centimeter allows for easy implantation of the radiation source around the tumor area, after the method of Paterson and Parker. The tubing, fed through needle guides, may also be used in the same manner as conventional radium needles. During surgery the radioactive source may be placed anywhere it is deemed necessary and long, stretched inactive ends of the nylon tubing brought out through a puncture wound in the manner of a drain, allowing for removal of the cobalt without further surgery. The diameter of the circular implant must exceed 4 cm. to prevent locking.—*M. B. Goodwin, M.D.*

Twombly, Gray H., and Schoenewaldt, Erwin F. Tissue localization and excretion routes of radioactive diethylstilbestrol. *Cancer*, March, 1951, *4*, 296–302.

Diethylstilbestrol was labeled with $C^{14}$ at a calculated activity of 1.86 microcuries per milligram. This was given subcutaneously to 25 mice, a dog,and a rabbit.

Diethylstilbestrol was absorbed rapidly and its metabolic products were excreted into the bowel through the bile with 70 to 85 per cent excreted in the feces. Fifteen to 30 per cent passed in the urine. Most of the substance had been excreted in a period of twenty-one hours after the time of injection. There were no significant amounts of diethylstilbestrol or its products eliminated in the expired air, assuming that it is excreted by the routes listed above before it can be broken down into a simple substance which would appear as expired $CO_2$.

The highest concentration of the substance was demonstrated in the liver with no selective absorption in the uterus, pituitary, or breast. The bones likewise were free of any detectable activity. Therefore, it was concluded that radioactive diethylstilbestrol was excreted without sufficient breakdown to show any significant storage in the body. This is a worthy observation considering the long half-life of radiocarbon.—*J. W. Wilson, M.D.*

Herve, André, and Govaerts, Jean. Étude de la distribution dans l'organisme du phosphate de chrome radioactif injecté par voie intra-vieneuse. (Study of the distribution in the organism of radioactive chromium phosphate injected by the intravenous route.) *Acta radiol.*, April, 1951, *35*, 257–264.

In a former article the authors published the results of their investigation of the urinary excretion of $P^{32}$ injected intravenously in patients afflicted with various neoplastic lesions, particularly leukemia, lymphosarcoma and Hodgkin's disease. The study was made at the Anti-cancer Center of the University of Liège with radioactive phosphorus obtained from the laboratories of Oak Ridge and Harwell. It was found that the urinary excretion of

$P^{32}$ varied considerably, depending on the type of lesion. In general, the amount of $P^{32}$ retained by the neoplastic tissues was insufficient to produce a complete destruction of the tumor masses.

In order to obtain a more selective and therapeutically more efficient agent the authors, stimulated by the work of Jones, Wrobel and Lyons, undertook a series of experiments with radioactive chromium phosphate ($CrPO_4$) which they prepared in a colloidal solution. In the present article, they describe the results of these experiments which were performed mostly in rabbits and in a few mice. The radioactivity of the various organs was measured with the aid of a Geiger-Müller counter (supplied by the Cyclotron Specialties Co., U.S.A.) 2 minutes, 2 hours, 72 hours, 7 days, and 18 days after the intravenous injection of the radioactive colloidal chromium phosphate. Owing to the difficulty of obtaining satisfactory specimens in animals, the urinary excretion of the phosphorus was also determined in 5 human patients. The findings are presented in detail.

It was noted that chromium phosphate deposited with predilection in the spleen and liver, the maximum accumulation being reached on the seventh day. The bone marrow and the lungs stored a lesser but by no means negligible amount of the substance. Radioautographs of the spleen and liver clearly demonstrated the degree of radioactivity present. When the injection was made subcutaneously or intramuscularly, no diffusion of the colloidal solution took place, the radioactivity remaining confined to the site of the injection.

In the human, 8.05 per cent of the total injected dose of the radioactive chromium phosphate was excreted by the kidneys during the first five days after injection. On the fifth day the excretion amounted to only 0.42 per cent of the original dose. The authors therefore believe that this constitutes proof of the excellent fixation of the radioactive substance. They have also injected intraperitoneally 3 mc. of chromium phosphate in 2 cases of carcinoma of the ovary with peritoneal metastases and ascites and found a urinary excretion of only 6 per cent during the five day period.

No conclusions can be drawn as yet in regard to the clinical therapeutic value of the method.—*T. Leucutia, M.D.*

Geffen, Abraham, Loevinger, Robert, and Wolf, Bernard S. Surface activity following administration of radioactive phosphorus. *Radiology*, June, 1951, *56*, 857–868.

Metabolically active tissues, *e.g.*, malignant tumors, show more rapid and greater uptake of radioactive phosphorus than does normal tissue. Such areas of activity on the surface of the body may be readily located by means of a Geiger-Müller counter. Deep areas cannot be located because the beta rays of the radioactive phosphorus have a very short range.

Thirty patients with malignant and non-malignant conditions near or on the surface of the skin were given on an average dose of 500 microcuries of $P^{32}$, and relative surface activities determined over a period of days.

The normal individual shows different surface activities at different points on the body, *e.g.*, the surface over the frontal bone shows approximately twice as much activity as that over the sternum; but paired areas correlate within 15 per cent. The surface activity over malignant cutaneous lesions is 2 to 5 times that over normal areas. Midline lesions require a base point of reference as determined from normal individuals, *e.g.*, the normal cervix shows a surface activity 3 to 4 times greater than that of the thigh while carcinoma of the cervix shows an activity of more than 6 times greater than that of the thigh. Metastatic axillary lymph nodes were too deep to be detected by this method.

To prove that the difference in surface activities was not due to circulating phosphate, red blood cells tagged with $P^{32}$ were administered to 1 patient. Such injection gave an entirely different picture from that produced by the injection of inorganic phosphate. Similarly, vasodilation and vasoconstriction, as produced by immersion of the hands in hot and cold water, did not alter the relative surface activities following the injection of inorganic phosphate.—*M. B. Goodwin, M.D.*

Biggs, Max W., and Kritchevsky, David. Observations with radioactive hydrogen ($H^3$) in experimental atherosclerosis. *Circulation*, July, 1951, *4*, 34–42.

The fate of exogenous and endogenous cholesterol in normal and hypercholesterolemic rabbits was studied. Tritium labelled cholesterol, with a stable tritium linkage, was prepared according to the method of Bloch and Rittenberg.

Tritium water injections showed that within about four hours body water specific activity reached an equilibrium value. At the end of one day the adrenal, kidney and aortic cholesterol showed no tritium contamination. Following daily injections, 6 additional animals were killed after a lapse of from two to thirty-nine days and specific activities in various tissues determined. All examined tissues showed activity.

Four rabbits were made hypercholesterolemic by feeding cholesterol. Two received labelled cholesterol while the other 2 received unlabelled cholesterol but their body water was kept labelled with tritium. It was thus shown that most of the tissue cholesterol, including aortic atheromas, was of exogenous origin. A small amount was of endogenous origin. Despite the massive oral doses some in vivo cholesterol synthesis still occurred. The fate of tagged oral chol-

esterol was further studied in a normal, resistant and 3 hypercholesterolemic rabbits. The resistant animal had no atheromas at death and had only a few "abnormal" circulating molecules. The hypercholesterolemic group were strongly positive for the Gofman $S_f$ 10–30 molecules and all had aortic atheromas at death.

Some data show that esterified serum cholesterol goes to higher levels sooner than free cholesterol.—*Z. S. Gierlach, M.D.*

Wrenn, Frank R., Jr., Good, Myron L., and Handler, Philip. The use of positron-emitting radioisotopes for the localization of brain tumors. *Science*, May 4, 1951, *113*, 525–527.

To date the most commonly used isotope for detection and localization of brain tumors has been $I^{131}$, incorporated in the dye diiodofluorescein. G-M tubes with lead shielding, for collimation and protection from backscatter, have been used.

Higher detection efficiencies of up to a theoretical 100 per cent can be obtained with scintillation counters. By also utilizing the fact that in positron annihilation 2 gamma-quanta are given off simultaneously in opposite directions, the source of activity could be further delimited. Single and coincidence scintillation counter results were compared with each other, and with a standard G-M tube under control conditions. For this purpose a radioactive, positron emitting point source (either $Zn^{65}$ or $Cu^{64}$) was suspended in air, or imbedded in a fixed brain within a skull. Counting rate curves, similar to those calculated on a theoretical basis, were obtained for the scintillation counters. A single directional scintillation counter gave a 47 fold increase in counting rate when compared with a Geieger tube under similar conditions. By using directly opposed uncollimated scintillation counters, the annihilation gamma pairs from the $Cu^{64}$ source permitted closer delimitation. When used with lead collimators, scattering was insignificant.

The radiocopper was incorporated into copper phthalocyanine (tetra-benzo-tetra-aza porphin), and experimental animal work carried out with doses up to 100 mg/kg.

Administration of this dye into experimentally produced brain injury demonstrated concentration in the damaged areas.—*Z. S. Gierlach, M.D.*

Lewison, E. F., Levi, J. E., Jones, G. S., Jones, H. W., and Silberstein, H. E. Tracer studies of radioactive sodium estrone sulfate ($S^{35}$) in cases of advanced breast cancer. *Cancer*, May, 1951, *4*, 537–548.

The authors analyzed the fate, excretion, and certain tissue concentrations of sodium estrone sulfate tagged with $S^{35}$. Six women with advanced breast cancer and 1 woman with advanced cervical cancer were studied.

The radioactive material was promptly excreted in the urine. The excretion rate was greatest in the first twenty-four hours. Over a seventy-two hour period from 70 to 99 per cent of the activity was eliminated by this route. The average of 4 cases was 80 per cent. The bulk of this was excreted as an inorganic sulfate fraction. A smaller amount was excreted as estrone sulfate and a very small amount in the ethereal form.

In 1 case 200 I.U. of prolactin daily for seven days reduced the first twenty-four hour urinary excretion from 62.1 per cent of the dose to 44.4 per cent of the dose.

Radioactive tissue concentration studies showed there was a comparative ratio of 14 times in tissue concentration of labeled estrone sulfate in breast cancer tissue over normal breast tissue. It should be noted that there was a ratio of 4.2 when the tagged sodium sulfate was administered. Other tissue studies showed variable concentrations but not as marked. The cervical mucosa showed the next most concentration.—*W. L. Bridges, M.D.*

Muller, J. H., and Rossier, P. H. A new method for the treatment of cancer of the lungs by means of artificial radioactivity ($Zn^{63}$ and $Au^{198}$); first experimental and clinical studies. *Acta radiol.*, May–June, 1951, *35*, 449–468.

The clinical development of selective fixation of artificial radioactive materials within the lungs is shown. $Au^{198}$ in the form of a precipitate with particle size 30–50 $\mu$ in a pectin-containing solution with the addition of heparinized blood of the patient is used. This is preferred to $Zn^{63}$ because of its longer half-life period. When given intravenously diffuse micro-emboli in the lung tissue are produced. The radioactivity can be localized to a certain part of the lung by injecting the radioactive solution into a catheter which has been inserted through the heart into a selected pulmonary artery. Up to 150 mc. has been injected in this way.

This procedure was carried out in 6 patients. $Zn^{63}$ was used in 2 patients and $Au^{198}$ in 4. One was a case of pulmonary metastases from a hypernephroma, 1 a pulmonary lymphogranuloma and 4 were inoperable bronchial carcinomas.

The method may be combined with intrapleural or intratumoral injections of colloidal $Au^{198}$ as well as with classical roentgen therapy or surgical operations.—*Mary Frances Vastine, M.D.*

Tubiana, M., and Süe, P. Interêt médical de l'examen topographique de la thyroide par mesure externe du radioiode. (Clinical significance of topographic study of the thyroid by means of external measurement of radio-

iodine.) *Presse méd.*, July 18, 1951, *59*, 1027–1029.

Since fixation of iodine in the thyroid is proportional to the activity of that gland, radioiodine can be used to measure the activity of the thyroid and of each of its parts. This is significant in distinguishing between benign and malignant thyroid nodules, since nodules showing an activity greater than the surrounding thyroid tissue never prove malignant, while about 20 per cent of all nodules with lower activity are malignant. Aberrant thyroid tissue in the chest or tongue can also be demonstrated.

The authors present a method with which the thyroid is mapped after ingestion of radioiodine. Measurements are made externally at points 4 mm. distant from each other, using a collimating counter of their own design, which is described and illustrated. Two patients with very similar clinical manifestations are briefly reported. Both had thyroid nodules, signs of mild hyperthyroidism, and impairment of general health; in 1 of them the nodule showed less activity than the surrounding tissue and proved to be malignant.—*Albert Oppenheimer, M.D.*

Blumgart, Herrman L., Freedberg, A. Stone, and Kurland, George S. Treatment of incapacitated euthyroid cardiac patients by producing hypothyroidism with radioactive iodine. *New England J. Med.*, July 19, 1951, *245*, 83–91.

This article reports 37 patients with stationary chronic heart disease of months or years duration treated by producing hypothyroidism with radioactive iodine. These patients were all euthyroid cardiac cripples; most of them were confined to bed, or were unable to undertake more than slight effort without developing angina pectoris or a recurrence of congestive failure.

The initial dose was calculated to deliver 30,000 to 50,000 equivalent roentgens to the normal thyroid. Measurements of $I^{131}$ uptake were made prior to the administration of the therapeutic dose and also subsequent to the same. Nine of the patients received one dose of $I^{131}$, 18 patients received two doses, and the remaining 10 patients up to six doses with 1 patient receiving the latter.

Twenty-three of the 37 euthyroid cardiac patients were followed in the hypometabolic state for seven to 26 months with an average of one and a half years. No serious toxic reactions occurred. Mild transitory hyperthyroidism was present in 2 patients and two-thirds of the patients experienced thyroiditis. These complications were controlled without difficulty.

One-third of the patients have shown remarkable improvement, one-third have improved somewhat, and in another one-third there was no improvement.

The authors attempted to maintain the lowest metabolic rate consistent with the comfort of the patient. Supplementary small doses of thyroid extract have been given after the induction of myxedema.

Hypothyroidism induced by radioactive iodine appears to be able to accomplish worthwhile improvement in selected cardiac patients without the inevitable risk and complications of surgery.—*F. J. Rigos, M.D.*

Schneeberg, Norman G., Perloff, William H., and Serber, William. With the technical assistance of Sopp, T. E., and Stanton, L. An evaluation of the radioiodine concentration test in the study of thyroid disease. *Radiology*, June, 1951, *56*, 869–875.

The purpose of this study was to determine the applicability of the radioactive iodine tracer test to the routine hospital examination of thyroid disease. One hundred microcuries of $I^{131}$ in 50 cc. of water, without added carrier iodine, were administered orally to patients one hour after a light breakfast, or in the fasting state, followed by 100 cc. of water. Counts of gamma radiation were made for five minute periods at five or six hours, twenty-four hours, and at forty-eight hours.

One hundred and fifty-nine patients were studied; they were placed in three groups: (1) "Normal" control group—115 patients; (2) hyperthyroidism—25 patients; and (3) hypothyroidism—19 patients.

The normal range of uptake of the administered dose was established between the limits of 10 per cent and 35 per cent. Thirteen per cent of the normal subjects were below and 10 per cent were above these limits. All of the hyperthyroid patients concentrated 35 per cent or more, and all of the 19 hypothyroid patients concentrated 10 per cent or less of the administered dose.

The radioiodine test was found to be more than twice as accurate as the basal metabolism rate, in the recognition of normal thyroid function, and was equal in the diagnosis of thyroid disease. It was found that a single twenty-four hour reading after the administration of $I^{131}$ was adequate for routine diagnostic studies.—*E. M. Cooper, M.D.*

Crile, George, Jr., and McCullagh, E. Perry. The treatment of hyperthyroidism; an evaluation of thyroidectomy, of prolonged administration of propyl thiouracil, and of radioactive iodine. *Ann. Surg.*, July, 1951, *134*, 18–28.

The authors feel that all three methods of treatment are safe and effective.

In 540 consecutive thyroidectomies, no deaths and few complications were encountered. This is accomplished by using an anatomic surgical approach, by adequate pretreatment and by selecting only good surgical risks. A five year follow-up shows only a 2.1 per cent recurrence of hyperthyroidism

while 21 per cent developed hypothyroidism. Surgery is most effective in toxic nodular goiter.

Propyl thiouracil treatment is justified in selected cases and for preoperative preparation. It is used primarily in small or medium sized diffuse goiters and in hyperthyroid patients whose life expectancy is poor. It is also used in those patients who remain as poor surgical risks despite adequate treatment. Nodular goiter, because of cosmetic effects, possibility of enlargment and/or malignancy, is best treated surgically.

In treatment with $I^{131}$ the authors calculate that by assuming a 50 per cent uptake of the usual 7 mc. therapy dose in a 50 gm. goiter about 7,000 equivalent roentgens will be delivered to the thyroid. All patients receive a tracer study before therapy. Experience gained from over 400 radioiodine treated patients leads the authors to conclude that when hyperthyroidism is controlled the patients are as well as when treated by surgery. It is stressed that to date no carcinomas have developed in radioiodine treated cases.

In 73 patients with Graves' disease the total dose for control was 14 mc. In nodular goiter with hyperthyroidism the average total dose was 42 mc.

The great advantage of $I^{131}$ therapy is that the patient remains ambulatory.—*Z. S. Gierlach, M.D.*

Hahn, P. F., Skipper, H. E., Carothers, E. L., and Bernard, L. J. The effect of radioactive colloidal metallic gold in the treatment of "acute" AK-4 leukemia in mice. *Cancer*, May, 1951, *4*, 634–636.

Since radioactive colloidal gold sols have produced uniformly favorable remissions in both chronic myelogenous and chronic lymphogenous leukemia in humans, the authors proposed to investigate their effects on the acute disease in experimental animals. Using AKm mice, a strain of mice in which acute leukemia can be induced, spleen cells from advanced cases of AK-4 strain of leukemia were injected intraperitoneally. Intraperitoneal inoculation with radioactive gold colloids was then used in treatment. Survival days of the experimental mice were compared with equal numbers of control mice.

With doses of radioactive gold of 0.1 to 0.2 mc., the life span of treated over untreated animals increased from 18 to 37 per cent. This compares with an increase in life span of 38.5 per cent when using 600 r of total body roentgen irradiation, 25 to 50 per cent when using urethane and nitrogen mustard and over 100 per cent when using the antifolics.

The authors have concluded after this work and limited use in acute leukemia in humans that radioactive gold, like other forms of treatment, such as urethane, nitrogen mustard and roentgen irradiation, is unsatisfactory for the treatment of acute leukemia. On the other hand, it sometimes produces longer term palliation in the chronic forms of the disease.—*D. E. Vivian, M.D.*

Osgood, Edwin E., Li, Jonah G., Tivey, Harold, Duerst, Marie L., and Seaman, Arthur J. Growth of human leukemic leucocytes *in vitro* and *in vivo* as measured by uptake of $P^{32}$ in desoxyribose nucleic acid. *Science*, July 27, 1951, *114*, 95–98.

It is possible to compare in vitro the rate of formation of human leukocytes in culture with that of the same population of leukemic cells in a patient who has leukemia. This is done by determining the uptake rates of radioactive phosphorus ($P^{32}$) into desoxyribose nucleic acid (DNA) and by parallel determinations in the cell-donor patient with leukemia treated with $P^{32}$. Radioactive phosphorus is incorporated in DNA principally during mitosis. The rate of cell formation supplements the information on the rate of cell differentiation, obtainable from total and differential cell counts, and the rate of mitosis obtainable with colchicine.

Leukocytes from patients with leukemia were isolated aseptically and introduced into culture medium. Daily samples were withdrawn and counted. At intervals of two days a large quantity of the mixed culture was withdrawn. The cells were packed and then the DNA was determined. The DNA phosphorus radioactivity was determined measuring the total $P^{31}$ and $P^{32}$.

When possible, parallel determinations of $P^{32}$ uptake in DNA were made in the patient and in culture. The $P^{32}$ level in the plasma of the patient depends upon the initial dose needed by that particular patient. To obtain equivalent radiation effects the $P^{32}$ content of the culture was made equal to the plasma level in the patient. Daily injections of one-tenth or less of the initial dose served to maintain the plasma $P^{32}$ level of the patient essentially constant.

The rate at which $P^{32}$ disappears from the DNA of cells cultured in $P^{32}$ free medium from a patient who has been previously treated with $P^{32}$ should be an equally good measure of the rate of cell death and autolysis and, if the cell count remains constant, of the rate of new cell formation. Since $P^{32}$ cannot be removed instantly from extracellular fluid, this technique cannot be employed in vivo.

Three attempts to culture the cells of patients with chronic lymphocytic leukemia failed to show significant uptake of $P^{32}$ in DNA over periods of time up to ten days, although uptake of $P^{32}$ in non-DNA fractions occurred. This result is to be expected in view of the uniformly slow rate of new DNA formation observed in vivo.

The slope of the uptake curve of $P^{32}$ in DNA in the cultures of cells from patients with chronic granulocytic leukemia indicates new cell formation of at least 20 per cent of that observed in the patient.

The data appear to demonstrate that growth of leukocytes from patients with chronic granulocytic or acute lymphocytic leukemias takes place in vitro

and that the rate of new cell formation can be estimated by the rate of uptake of $P^{32}$ in the DNA fraction, either in vivo or in vitro.—*F. J. Rigos, M.D.*

## CHEMOTHERAPY

Bierman, Howard R., Kelly, Keith H., Dod, Kenneth S., and Byron, Ralph L., Jr. Studies on the blood supply of tumors in man. I. Fluorescence of cutaneous lesions. *J. Nat. Cancer Inst.*, April, 1951, *11*, 877–890.

This report deals with studies in vivo of the afferent blood supply of neoplasms and other lesions in the skin as demonstrated by fluorescein.

Three to 10 cc. of 5 per cent fluorescein was injected rapidly into a major artery leading directly toward the tumor site. The time of appearance and duration of the fluorescence was observed under ultraviolet light.

Eighteen patients with cutaneous lesions were studied. The vascularity was increased in all lesions, the degree of increase being less in those lesions having necrotic changes on the surface. Lesions of mycosis fungoides and lymphoepithelioma fluoresced more promptly and brighter.

Previous surgery, roentgen irradiation and nitrogen mustard therapy decreased the fluorescence.

It is suggested that some chemotherapeutic agents may be more advantageously given via the arterial route, delivering higher concentrations directly to neoplastic tissue.—*V. L. Peterson, M.D.*

Bierman, Howard R., Kelly, Keith H., Byron, Ralph L., Jr., Dod, Kenneth S., and Shimkin, Michael B. Studies on the blood supply of tumors in man. II. Intra-arterial nitrogen mustard therapy of cutaneous lesions. *J. Nat. Cancer Inst.*, April, 1951, *11*, 891–906.

The arterial blood supply of some cutaneous neoplasms has been shown to be increased, affording a direct route for administration of chemotherapeutic drugs. In addition, the capillaries within some neoplasms possess permeability that allows the prompt and prolonged appearance of fluorescein and certain radioisotopes in lesions.

The increased vascularity of tumors permits exposure of a large volume of tumor to relatively high concentrations of nitrogen mustard when administered directly into the arteries supplying the tumor. This was considered the most important factor for the more marked clinical improvement observed following intra-arterial rather than intravenous nitrogen mustard.

There were fewer systemic changes following arterial than intravenous injection of nitrogen mustard.

Twenty-seven intra-arterial and fifteen intravenous injections of nitrogen mustard ($HN_2$ were given in 17 hopelessly incurable patients with cancer involving the skin.—*V. L. Peterson, M.D.*

Karnofsky, D. A., Burchenal, J. H., Armistead, G. C., Jr., Southam, C. M., Bernstein, J. L., Craver, L. F., and Rhoads, C. P. Triethylene melamine in the treatment of neoplastic disease; a compound with nitrogen-mustard-like activity suitable for oral and intravenous use. *Arch. Int. Med.*, April, 1951, *87*, 477–516.

The nitrogen mustard methyl-*bis* (2-chloroethyl) amine hydrochloride ($HN_2$) has been widely used for five years as a palliative agent in the management of certain neoplastic diseases. Disadvantages include the necessity for intravenous administration, the production of nausea and vomiting, the painful local reaction which follows extravasation, venous thromboses, and the severity of bone marrow depression.

Research has been directed toward finding a nitrogen mustard with a greater selective effect on tumor as compared with normal tissue and toward obtaining a derivative which can be administered more conveniently. The former effort has, so far, not been successful, but progress has been made toward the latter through the discovery of the tumor-inhibiting effects of triethylene melamine (2,4,6-triethylenimino-5-triazine). This nitrogen mustard derivative, after promising animal experimentation, was given a therapeutic trial with humans.

It has toxicological and therapeutic properties similar to those of methyl-*bis* (2-chloroethyl) amine hydrochloride ($HN_2$) but is more active by weight and does not produce central nervous system or cholinergic stimulation at $L.D._{50}$.

The intravenous use produces transient improvement, similar to that obtained with the nitrogen mustard, in Hodgkin's disease, lymphosarcoma, and chronic lymphatic and myelogenous leukemia. It rarely causes nausea, vomiting, or venous thromboses, but it depresses the bone marrow as severely as the nitrogen mustard.

Triethylene melamine is an effective therapeutic agent when given by mouth. It produces only slight nausea and occasional vomiting. Oral therapy has produced temporary clinical improvement in persons with Hodgkin's disease, lymphosarcoma, chronic lymphatic and myelogenous leukemia, and mycosis fungoides.—*George Cooper, Jr., M.D.*

Dacie, J. V., Dresner, E., Mollin, D. L., and White, J. C. Acute leukaemia treated with a-methopterin. *Brit. M. J.*, April 14, 1951, *1*, 784–792.

The authors corroborated the dissappointing results obtained with the antifolic derivatives, in this case a-methopterin, in treating acute leukemias. Their series of cases consisted of 2 adults and 5 children. The toxic reactions to this drug were severe and rendered the treatment hazardous. The amount of a-methopterin needed to influence the marrow

varied enormously in that a severe reaction occurred after only 10 mg. of a-methopterin in one case, whereas 120 mg. was needed in another case to cause significant alteration of the white cell count. In all cases severe hemorrhagic complications occurred. The unusual feature of bleeding from the middle ear was noted in 2 instances. The authors believed that the hemorrhagic complications were responsible for the death of 6 of these patients. Significant remission was only obtained in one child with acute lymphoblastic leukemia. This remission was of short duration. The writers supported previous reports in the literature in that the cause of the hemorrhagic diathesis was probably not secondary to heparin-like substances in the blood. Also, the extensive gastrointestinal ulcerations found at the autopsy of these patients were thought to be a primary leukemic manifestation.

The authors postulate that the citrovorum factor of Sauberlick might be helpful in counteracting the toxic effects of the folic acid antagonists in human leukemia but as yet this has not been tried.—*T. D. Allison, M.D.*

Godwin, John T., and Escher, George C. Hormone-treated primary operable breast carcinoma; pathological study of thirty-three cases. *Cancer*, Jan., 1951, *4*, 136–140.

This study was instigated as the result of one instance of marked diminution in size of a primary breast carcinoma after testosterone therapy initially regarded as inoperable, sufficient to make the tumor at least technically operable. The paper deals with an additional 32 cases in which the breast was removed by radical surgery following twenty-eight days of steroid hormone therapy. Fifteen patients were androgen treated, 18 patients were estrogen treated.

It is emphasized that the tissue specimens must be of sufficient size to furnish a reasonable bulk of tissue for study. Small skin biopsies or postmortem material are unsatisfactory for proper evaluation.

Representative sections of all treated cases and an equal number of untreated cases were sent to several pathologists, none of whom succeeded in distinguishing one group from the other to a degree regarded as significant beyond the realm of chance. The degree of fibrosis and cytoplasmic vacuolization appeared more prominent in a few instances than would have been expected in non-hormone treated cases.

The mode or mechanism of the effect of steroid hormones on breast carcinoma is unknown. It would appear that the effect of hormones is such that some of the tumor cells are destroyed and scarring results.

Clinically, 9 of the estrogen treated group exhibited measurable reduction in the primary mass dimensions. Twelve cases presented palpable axillary lymph nodes, none of which demonstrated clinical regression.

Seven of the 15 patients treated with testosterone exhibited measurable reduction in the size of the primary tumor. Six had palpable axillary lymph nodes prior to treatment. Following hormone therapy, these lymph nodes were no longer palpable in one case and reduced in size in another.—*W. Little, M.D.*

Campbell, J. H., and Cummins, Sam D. Metastases, simulating mammary cancer, in prostatic carcinoma under estrogenic therapy. *Cancer*, March, 1951, *4*, 303–311.

In reviewing the literature, the authors found 11 reported cases of carcinoma of the breast in man, developing during the course of estrogen therapy for disseminated prostatic cancer. In all but 1 case the disease was regarded as originating in the breasts and initiated by estrogens.

The diagnosis of the breast lesions as being primary cancers was based entirely on histopathology. Carcinoma of the prostate is quite anaplastic and produces metastases which may differ markedly from the parent lesion.

The authors report a case of prostatic cancer with metastasis simulating breast cancer and base this report on the fact that the cytoplasm and nucleus of the metastatic breast lesion were stained dark brown by the lead sulfide in the acid phosphatase method of Wolf, Kabat and Newman. The metastatic lesions were present in both breasts.

The authors question whether estrogens induce breast carcinoma in man during therapy for disseminated prostatic carcinoma.—*W. L. Bridges, M.D.*

Segaloff, Albert, Gordon, Douglas, Horwitt, Benjamin N., Schlosser, Joseph V., and Murison, Paul J. Hormonal therapy in cancer of the breast. 1. The effect of testosterone propionate therapy on clinical course and hormonal excretion. *Cancer*, March, 1951, *4*, 319–323.

In the present study an attempt was made to evaluate the effect of testosterone propionate therapy on hormone-excretion patterns in patients with cancer of the breast and to correlate the effects with the clinical course.

All patients under study received 100 mg. of testosterone propionate in vegetable oil either three times weekly or every other day. An attempt was made to evaluate hormonal patterns before and during therapy. Urinary excretion of 17-ketosteroids, gonad-stimulating hormones, lactogenic hormone (prolactin), glycogenic corticoids, and urinary creatine-creatinine ratios were measured.

Forty-eight patients were treated with testosterone propionate. Their ages ranged from six to seventy-five years, with thirty-five more than forty years of age. The majority had known of the presence of the

tumor less than five years. All but 2 patients had received surgical therapy, irradiation, or both, to the initial lesion. Almost all patients had undergone the menopause, either normally or by surgical or roentgenological castration.

Thirteen of the 48 patients, or 27 per cent, showed objective regression of lesions. The duration of regression extended over an average period of 31.3 weeks, the longest being fifty weeks. In none of the 10 patients less than forty years old was a good response obtained, whereas a third of those more than forty years old showed improvement. No correlation was noted between the type of menopause experienced and the therapeutic results obtained, except that the patients who were still menstruating gave uniformly poor results.

In the excretion studies all patients showed an expected increase in 17-ketosteroid excretion as well as an expected decrease in gonad-stimulating hormone excretion. In the patients who showed improvement, there was a decrease of doubtful significance in urinary corticoids, and conversely an increase in corticoids in the patients who did not show improvement. Prolactin excretion for both groups of patients increased.

In general, the patients who improved showed a decrease in urinary creatine, whereas those who failed to improve showed an average increase in urinary creatine. The authors feel that the fairly uniform finding of creatinuria in patients of both groups is a reflection of the destruction of body protoplasm, by the invading neoplasm. The failure of the creatinuria to decrease in the unresponsive patients probably reflects further destruction of body tissue, whereas the striking decrease in creatinuria observed in patients showing a good therapeutic result is a reflection of the reparative tissue process as well as a decrease in the destructiveness of the neoplasm.—*F. R. McCrea, M.D.*

Nathanson, Ira T. Sex hormones and castration in advanced breast cancer. *Radiology*, April, 1951, *56*, 535–552.

Hormone therapy can be considered as another weapon in the treatment of breast cancer. Its field of usefulness is chiefly as an adjunct to surgical and radiation therapy. It may also be utilized as an initial therapeutic measure for selected advanced primary lesions beyond the scope of effective surgical or radiological attack. The effects are temporary and usually of short duration. Permanent control of even the most susceptible breast cancers should not be expected.

Discussed are castration, androgens, estrogens and other hormones such as progesterone, cortisone and adrenocorticotropic hormone. Gross and microscopic changes in the primary tumor following hormone therapy and in lymph node, osseous, pulmonary and hepatic metastases are enumerated.

Androgens appear to be most efficacious in the production of favorable effects on osseous metastases. In premenopausal women castration is generally more beneficial than androgen therapy, presumably because of more complete suppression of ovarian function. Effective suppression of ovarian function in the average patient does not occur before a minimum of six or eight weeks after irradiation. Ovariectomy is therefore preferable if a rapid effect is desired.

Estrogens are indicated for advanced primary breast cancer and its distant deposits in post-menopausal women, regardless of chronologic age. Best results are obtained in elderly patients. Acceleration of the disease may occur in premenopausal women. In the menopausal group variable responses, ranging from acceleration to remission, may be observed.

Late changes in the tumor bed following regression of the lesion with estrogen therapy are similar to those occurring after irradiation. Radiation therapy to areas of reactivation of the tumor in these sites must be applied with the same caution as if they had been previously irradiated.

Proper precautions must be taken when sex hormones are used in breast cancer because of possible serious complications. Unfavorable systemic effects common to estrogens and androgens are nausea and vomiting, edema and hypercalcemia. Uterine bleeding and urinary frequency and incontinence may occur when estrogens are used. Hirsutism, acne, hoarseness and increased libido may occur with androgen therapy.—*A. W. Sommer, M.D.*

Burchenal, J. H., Karnofsky, D. A., Kingsley-Pillers, E. M., Southam, C. M., Myers, W. P. Laird, Escher, G. C., Craver, L. F., Dargeon, H. W., and Rhoads, C. P. The effects of the folic acid antagonists and 2,6-diaminopurine on neoplastic disease, with special reference to acute leukemia. *Cancer*, May, 1951, *4*, 549–569.

This complete report deals with the results obtained in treatment of neoplastic disease with antimetabolites. The substances used are discussed as to chemistry and effects on experimental animals. They include the 4-amino-pteroylglutamic acid derivatives (aminopterin, amethopterin, aminoanfol, etc.) and 2,6-diaminopurine. The latter, an antagonist of adenine, has been shown to be effective against mouse leukemia, and even a subline of leukemia made resistant to amethopterin. For this reason, it was felt that its mechanism of action was somewhat different from the antifolics and that it might be useful in some cases which failed to respond or had become resistant to them.

All of these compounds are extremely toxic and must be administered with caution. In most instances, it is necessary to administer the drugs until toxic symptoms appear, before desired effects are

obtained. Both continuous and intermittent courses were given, the intermittent in hopes that it would prove to be a more effective technique.

The signs of toxicity, in relative frequency and usual order of appearance are as follows: (1) mouth lesions; (2) intestinal ulceration, diarrhea and bleeding; (3) leukopenia, thrombocytopenia, and anemia; (4) increased susceptibility to infection; (5) skin rash; (6) alopecia.

In their series, it was the authors' policy to treat with the antagonists until remission occurred or definite signs of toxicity appeared. When toxicity occurred, treatment was stopped, and resumed later at a lower dose.

One hundred sixty-two patients were studied in the original group and 47 additional patients with acute leukemia have been treated with amethopterin since (no real therapeutic advantage of one folic acid antagonist over another was detected).

Good clinical and hematological remissions were seen in 32 per cent of 97 children and 2.6 per cent of 38 adults with acute leukemia.

The use of 2-6 diaminopurine produced favorable response in 4 patients with leukemia, but failed in 25 others.

Clinical improvement was noted in 3 of 7 children with lymphosarcoma, and in both of 2 children with generalized reticulo-endotheliosis, treated with antimetabolites.

No consistent beneficial effects were noted in the various other diseases treated which included chronic lymphatic leukemia, Hodgkin's disease, mycosis fungoides, plasma cell myeloma, and carcinoma of the breast.—*R. A. Silver, M.D.*

McClure, James A., and Higgins, Charles C. Bilateral carcinoma of male breast after estrogen therapy. *J.A.M.A.*, May 5, 1951, *146*, 7–9.

Cancer of the male breast developing coincident with or after estrogen therapy is an unusual occurrence. Few cases in the literature are recorded. A questionnaire was sent to 150 urologists asking whether or not breast cancer was observed in any patient treated with estrogens for prostatic cancer. Of a total of approximately 17,000 patients treated, only 1 additional possible case of cancer of the male breast was reported.

A fifty-six year old white man entered the Cleveland Clinic on June 6, 1950, for investigation of a lesion of the urinary bladder. A cystoscopic examination revealed a malignant tumor of the bladder, and a suprapubic transvesical resection with electrofulguration of the tumor base was performed.

On microscopic examination, the tumor proved to be a transitional cell carcinoma of Grade 2 malignancy with squamous metaplasia. The patient was subjected to two courses of deep roentgen therapy over a five month period, receiving 4,400 r (in air) to the anterior bladder, 4,200 r to the left posterior oblique, 4,100 r to the right posterior oblique, 1,200 r to the right anterior oblique and 900 r to the left anterior oblique fields. For palliative treatment of suprapubic pain, estrogen therapy was administered at the Verterans Hospital. For fifty-one days an oral daily dose of 15 mg. of diethylstilbestrol was given, making a total of 765 mg. He then received orally 5 mg. of diethylstilbestrol daily for a total of 375 mg. Also a daily dose of 5 mg. of estradiol (ovocylin) dipropionate was given intramuscularly for 126 days, or a total of 630 mg. Thus during the entire period of 126 days, the patient received 1,770 mg. of estrogens. Six weeks prior to the cessation of estrogen therapy, swelling and tenderness of both breasts were noted. These progressively increased even after all estrogen therapy had been discontinued. The breast became hard, tender, and about the size of a lemon, until admission to the Cleveland Clinic Hospital.

Retraction of the nipples was observed, but no axillary lymphadenopathy was evident. Prostatic examination revealed a hard, fixed prostatic bed with a broad base suggestive of a bladder neoplasm with extravesical extension.

Breast biopsies were performed, and histopathological examination showed the specimens from both right and left breasts to be similar, representing carcinoma simplex, Grade 4. The patient's hospital course has been one of progressive weakness.

It is of interest that the breast malignancies were bilateral new growths, histopathologically different from the primary neoplasm. No breast disease was ever noted prior to the administration of estrogens. A family history of mammary and other carcinomas suggests the possibility of activation of male breast malignancy in a patient having a family strain of relatively high cancer incidence. All male patients receiving estrogen therapy should therefore, be questioned about their family history relative to breast malignancy. The character of the breasts should be carefully evaluated prior to and at regular intervals during estrogen therapy.

The interpretation of the actual relationship of the breast cancer and estrogen therapy is difficult.—*S. N. Tager, M.D.*

## MISCELLANEOUS

Taplin, George V., and Douglas, Clayton H. A colorimetric dosimeter for qualitative measurement of penetrating radiations. *Radiology*, April, 1951, *56*, 577–591.

When considering the problem of handling évacuées from the vicinity of an atomic blast, a knowledge of the approximate amount of radiation received by the individual would be invaluable because clinical signs of radiation injury are not manifest immediately. A division of the total body irradiation into ranges of 0–200 r, 200–400 r, and 400–600 r is

believed to be of clinical value, hence an évacuée carrying an indicator showing the amount of radiation to which he has been exposed may be readily classified. Several such indicators are discussed with respect to their reliability, stability, sensitivity, cost, and ease of interpretation in an attempt to improve upon the well known film badges which must be developed and interpreted with a densitometer. A chemical method based on the evolution of acid from an aqueous solution of chloroform was found to be the most promising, stability above 37° C. requiring a two-phase system.

The acid liberation, which is directly proportional to the amount of a given quality of radiation, reduces the pH of the aqueous phase, containing the indicator bromcresol purple, which turns from purple at pH 6.8 to yellow at pH 5.2. By using a two-phase system, chloroform overlayed with the aqueous dye in the ratio of 15 parts chloroform to 1 part water, and concentrations of dye varying between 9.0 and 30.0 per cent, it is possible to measure three ranges of gamma dosage. A 9.0 per cent concentration of dye changes color completely at approximately 200 r (±50 r), a 20.0 per cent dye mixture at approximately 400 r, and a 30 per cent dye mixture at approximately 600 r.

The reaction shows a marked wavelength dependence, twice as much acid being produced by the same quantity of radiation having an average wavelength of 0.2 angstrom than that having an average wavelength of 0.1 angstrom. Fortunately, this dependence appears to be linear, making extrapolation to other than the standardization wavelengths possible. The rate of exposure does not affect the total amount of acid produced within the limits tested. A higher temperature during exposure will produce more acid per roentgen but this error is relatively small.

Three types of casualty dosimeters are described, a pencil type, a dog tag type, and an area monitoring type.—*M. B. Goodwin, M.D.*

Rosenthal, M., and Traut, H. F. The mucolytic action of papain for cell concentration in the diagnosis of gastric cancer. *Cancer*, Jan., 1951, *4*, 147–149.

The authors present a method of cell concentration using a solution of papain and cysteine hydrochloride for gastric lavage. Experimental studies on rats and clinical studies on 70 patients including clinically diagnosed gastric ulcers showed no untoward effects.

The authors report that food particles, sputum cells, salivary material and mucous strands are almost completely absent, while the gastric cellular return is uniformly abundant without noteworthy cellular degeneration.

Five of the 70 patients showd abundant malignant cells singly and in clumps with uniform distribution over the slides.

No cases known to have carcinoma or with a clinical diagnosis of carcinoma have been missed by this method up to the present time.—*W. L. Bridges, M.D.*

West, Philip M., Rapaport, Samuel I., and Tempereau, Clinton E. Enzymatic evaluation of therapeutic agents in cancer. *Cancer*, Jan., 1951, *4*, 177–183.

The purpose of this paper is to call attention to a method for evaluation of a palliative agent for cancer. In cases where objective evaluation of the progress of tumor growth is difficult, such a method is of great value.

The serum concentration of proteolytic enzyme inhibitors has been found to vary in many abnormalities, including malignancies. Two of these inhibitors, antichymotrypsin and antirennin, are discussed here. It has been found that a high antirennin level with a low antichymotrypsin level is associated with clinical evidence of arrested growth or tumor regression, while the reverse is found when tumor growth is progressing actively. The balance between these two values is of greater aid than the absolute value for either one. The reasons behind this are unknown. This test is applicable only when the existence of a malignancy has already been proved and there are no complications present that have been shown to influence the antienzyme pattern.

It is noted that this antienzyme balance seems to be a measure of neoplastic activity only, and not an indication of its extent, nor does it have any prognostic value.

There is hope that the relationship between the antienzyme balance and the status of the patient may provide an objective method for selection, evaluation, and more effective use of palliative agents in cancer.

Five sample patients taken from more than 400 cases studied by this method are presented. These cases all exhibited neoplastic lesions that permitted accurate evaluation of tumor growth or regression and all showed a marked parallelism between tumor growth and the antienzyme patterns.—*W. Little, M.D.*

Skipper, Howard E., and Mitchell, Jack H., Jr. Effect of roentgen-ray radiation on the biosynthesis of nucleic acids and nucleic acid purines. *Cancer*, March 1951, *4*, 363–366.

In view of the heterogeneous agents which may be used in cancer control including roentgen rays it has become increasingly important to try and determine if a single biological system in the cell is involved. It is known that nucleic acid synthesis is profoundly affected by folic acid antagonists.

The present study is an attempt to evaluate the effect on this by the use of roentgen rays. Hevesy has already observed that roentgen irradiation inhibited the incorporation of $C^{14}$ into desoxyribosenucleic acid (DNA) purines. The authors checked this and

extended this investigation. The complete experimental method is given and the results confirmed Hevesy's conclusions satisfactorily.

A dose of 950 r was given to the mice and the studies made with reference to $C^{14}$ demonstrated the inhibition of the incorporation of radioactive carbon from sodium bicarbonate and sodium formate into viscera nucleic acids and nucleic acid purines.—*J.S. Scott, M.D.*

Wilson, Philip D. Follow-up study of the use of refrigerated homogenous bone transplants in orthopaedic operations. *J. Bone & Joint Surg.*, April, 1951, *33-A*, 307–323.

This paper is a study of the results of the use of homogeneous bone grafts which had been preserved by refrigeration at temperatures of between minus 10 and minus 20 degrees centigrade for varying periods of time. The method of bone preservation is described and complications of wound healing are tabulated. Results obtained in spine fusions, filling of bone cavities, osteomyelitis, joint arthrodesis, ununited fractures and in some miscellaneous operations are summarized. The problems in the operation of a bone bank are briefly discussed. The following are the author's conclusions:

1. With careful technique, homogeneous bone grafts may be preserved for long periods of time.

2. Such grafts are well tolerated by human tissues and the risk of infection is no greater than with autogenous grafts.

3. The healing of such grafts takes place by a process of invasion, absorption, and replacement similar to that of autogenous bone grafts.

4. The results obtained are identical with those from the use of autogenous grafts, except that in some instances the healing appears to be a little slower.

5. The operation of a bone bank is safe and practical. It offers great advantages to the patient and the surgeon from the standpoint of availability, abundance, and the elimination of the necessity of a secondary operation to obtain bone.—*R. S. Bromer, M.D.*

Nickel, Allen C., Berger, Richard, and Brickley, Phyllis. The "Bolen test" in the diagnosis of neoplasms. *Am. J. Digest. Dis.*, May, 1951, *18*, 150–151.

The authors followed the technique described by Norman and Slicher as closely as possible. They found that when the Bolen test was definitely negative, especially on more than one occasion, it was very good evidence than no recognizable neoplasm was present at that time. When positive repeatedly, especially with large "lake areas", a malignancy should be looked for diligently. False positives were obtained in pregnancy, active tuberculosis, diseases of the female reproductive system, active thyroid conditions, when the serum bilirubin was two or more, active inflammatory processes, moderate secondary anemia, myocardial degeneration with early decompensation, quiescent arthritis and hypertension with associated lower nephron nephrosis.—*A. E. Childe, M.D.*

Lenzi, Mario, and Colombo, Siro. Tubo roentgen polianodico. (Polyanode roentgen tube.) *Radiol. med.*, May, 1951, *37*, 411–412.

The authors present a new roentgen tube. Its essential feature is that it has 8 anticathodes mounted concentrically on a circular support, the corresponding 8 spiral cathodes being in the center of the support. The tube can be operated with all or several anticathodes simultaneously, or with a single anticathode in rapid rotation. The roentgen beam may be considered for practical purposes as cylindrical or inversed conical, depending on the location and aperture of the collimating diaphragms used outside the tube.

For many years attempts have been made to design roentgen therapy tubes with a wide emission surface. Among these were the transparent anticathode tube of Wieser (1914), the annular anticathode tube of Bossi (1946), the tetrafocal tube of Palmieri (1941), and the conical anode tube of Sievert-Lindell-Wahlberg (1950).

One of the authors (Lenzi) since 1940 experimented with tubes based on the principle of Bragg's reflexion to obtain a roentgen beam converging outside the tube. The present tube, constructed differently, seems to solve the problem; it may also replace some of the mechanical arrangements currently used in therapy to increase the surface of the irradiation, as for example, the horizontal rotational method of Green, Jennings and Bush, the spiral rotational method, etc.—*T. Leucutia, M.D.*

Janker, R. Ein neues Rollfilm-Seriengerät für Röntgenaufnahmen im Format 30×30 cm. (A new roll-film serial apparatus for roentgenograms 30 by 30 cm. in size.) *Röntgen-Blätter*, May, 1951, *4*, 132–138.

An apparatus is described and illustrated whereby a 30 cm. wide, 20 meter long film strip runs between two screens and exposures made automatically at the rate of 5 per second. Thus 36 sequential roentgenograms can be made in a period of 7.27 seconds. Using per-abrodil, the author has utilized this rapid filmer in cerebral angiography and angiocardiography. The illustrated frames show good detail of the contrast substance and visualized structures.—*Harold Fulton, M.D.*

Büchner, H. Orthodiametrie. Teil I. Die Grössenbestimmung mittels einfacher Röntgendurchleuchtung. (Orthodiametry. Part I. Estimation of size by means of simple fluoros-

copy.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, May, 1951, *74*, 498–511.

A new procedure for the direct measurement of deep-seated objects is described. Two simple devices are added to conventional roentgenographic equipment: (1) a non-opaque, plastic disc containing a metal scale is attached to the fluoroscopic screen between the latter and the patient; (2) a light source, independent of the rest of the apparatus, casts a narrow beam on the screen. The screen and tube are so coupled together that they move in planes parallel to each other. The central ray coincides with the center of the screen.

To determine the transverse diameter of the heart, the procedure is as follows: (1) The "zero-point" is placed at one end of the desired diameter, so that the "zero-line," erected as a perpendicular to the "zero-point" on the scale, is tangent to the heart border; (2) the beam of light is superimposed on the "zero-line" and remains fixed; (3) the tube and screen are shifted so that the "zero-line" now lies tangential to the opposite heart border. The true diameter, the distance between the "zero-line" and the beam of light is obtained directly from the scale. The degree of distortion is also easily ascertained by measuring the excursion of the screen.

Other possibilities will be the subject of another paper.—*J. Zausner, M.D.*

Maxfield, J. R., Jr. Pneumoperitoneum in the study of pelvic structures. *J.A.M.A.*, July 7, 1951, *146*, 920–923.

In spite of the few untoward effects of pneumoperitoneum, the examination has not become popular. The author believes that it is a simple diagnostic procedure that should be available in all leading roentgenologic departments. The technique is briefly outlined and case reports are summarized to illustrate the information that can be derived from the procedure. The illustrations presented show gross pathologic changes which would seem to be recognizable on physical examination of the patients. Roentgenologic confirmation of the extent of the pelvic processes is undoubtedly of great value.—*R. E. Kinzer, M.D.*

Riley, Gardner M., Behrman, S. J., and De Vore, B. A simplified silver impregnation method for vaginal smears. *Science*, May 18, 1951, *113*, 574–576.

Feeling that the adherence to the staining method developed by Papanicolaou for the diagnosis of vaginal smears has permitted a standardization of technique and facilitated teaching, but has discouraged the application of other histological methods, the authors have developed a simple technique of silver impregnation for vaginal smears that will identify the chromatin elements of the nucleus.

The accuracy of the method was found to compare favorably with that of polychrome methods and the following are its technical advantages: (1) safe, simple, inexpensive and rapid; (2) counterstains are unnecessary; (3) the masking effect of erythrocytes is avoided; (4) smears are less fatiguing to examine than polychrome stained smears; (5) chromatin elements are deeply stained with silver.

Those interested in the technical details of the method are referred to the original article.—*F. E. O'Neill, M.D.*

Gebauer, A. Diagnostische Vorteile und Indikationsstellung der Körperschichtaufnahmen in transversalen Ebenen gegenüber denen in vertikalen. (The diagnostic advantages and indications for body section roentgenography in the transverse plane compared with the vertical.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, July, 1951, *75*, 9–21.

The author compares longitudinal laminagraphy in the frontal and sagittal planes with transverse laminagraphy and discusses the indications for transverse laminagraphy. He feels, that both are important, but the longitudinal body section seems preferable when examining organs that lie chiefly in the long axis of the body, such as the large bronchi, trachea, vertebral column, sternum, kidneys or when diffuse processes are present spreading in the horizontal plane.

In contrast to this, the transverse laminagraphy is better for appreciation of space and depth as regards the anteroposterior diameter, and gives more information as to the relationship of certain processes to the normal skeletal parts and normal soft tissue organs. The laminagrams delineating the retrocardiac space and pleural sinuses are excellent. The author calls these the "dead angles" of the longitudinal body section.

Ideally, a combination of cuts in both planes produces the more valuable study.—*P. C. Swenson, M.D.*

Takahashi, Shinji, and Shinozaki, Tatsuyo. Über zwei Methoden der Kymographie des Herzens in seinem horizontalen Querschnitt (Studien über Rotatographie, 5. Bericht). (Concerning two methods of kymography of the heart in horizontal section; studies of rotation kymography, fifth report.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, July, 1951, *75*, 1–8.

The authors describe two methods of roentgen kmyography for study of the heart in horizontal cross-section.

The first method is an intermittent or what they

call a discontinuous rotation kymography which gives a "stufen Kymogram," which might be described as a "graded" image of the heart in its cross-section.

The other they call a continuous rotation kymography, which gives a sort of composite picture of the heart in its cross-section. They claim that this method is of great advantage in getting more accurate interpretation of the true motions of the heart in its cross-section.

They have performed both methods on the abnormal as well as on the normal heart. From their findings they reconstruct a diagram of a cross-sectional plane of the heart which tells them a good deal more about the form, size and action of the heart chambers than does the ordinary kymogram. By analysis of their film findings and reconstructed diagrams, they can pick out more precisely the extent of the chambers and the site of the septa, and are able to gain a more accurate idea of the amplitude and character of the contraction waves of the heart. —*P. C. Swenson, M.D.*

Jacobson, L. O., Simmons, E. L., Marks, E. K., and Eldredge, J. H. Recovery from radiation injury. *Science*, May 4, 1951, *113*, 510–511.

Within twenty-eight days, 50 per cent of mice will be killed by a total body dose of 550 r ($LD_{50}$). If the surgically exteriorized spleen is shielded the required $LD_{50}$ dose is practically doubled. Similar shielding of the liver, or intestine, the entire head, or a hind limb, enhances survival and hematopoietic recovery, but to a lesser degree. Shielding of one exteriorized kidney has no effect on tissues or survival.

Surgical removal of the shielded spleen five minutes after 1,025 r has no effect on survival (0 per cent). If removed one to six hours after irradiation, survival is 66 per cent. Extirpation two days after roentgen exposure gives a survival of 39 per cent.

Normal splenic tissue transplanted into unshielded mice after 1,025 r total body dose significantly increased survival and tissue recovery. Early transplantation is most effective.

It is felt unlikely that "(1) cells migrate out from the shielded or transplanted tissue and are responsible for the enhancement of recovery, or (2) that irradiation of tissue produces a 'toxin' and that the shielded or implanted tissues exert a direct detoxifying action upon contact with the 'toxin'."

An attempt is being made to isolate the involved factor which (unlike cysteine, glutathione, anoxia or cyanide) is definitely effective after irradiation.—*Z. S. Gierlach, M.D.*

Friedman, Edward W., Frank, Howard A., and Fine, Jacob. Portal circulation in experimental hemorrhagic shock; in vivo roentgen ray studies. *Ann. Surg.*, July, 1951, *134*, 74–79.

The authors used roentgen methods in vivo in dogs to demonstrate changes in caliber of the portal and hepatic veins. The portal vein was demonstrated by 25 per cent thorotrast after catheterization of the splenic vein; the left hepatic vein and its branches were visualized by catheterization of the jugular vein and the inferior vena cava.

Hemorrhagic hypotension produced a decrease in cross-sectional area to 10 to 55 per cent of normal. The portal vein appeared to shorten as well as constrict. After blood volume replacement there was widening of the vessels from 38 to 88 per cent of normal with constriction again in a few hours to 63 per cent of original caliber. Further fluid replacement did not induce widening of the vessels.

Dibenamine was the sole agent to cause a substantial widening of the veins regardless of the stage of shock.

Similar findings, but to lesser degree, were noted in the hepatic veins.

The authors conclude that portal and hepatic venous constriction follows hemorrhagic shock and that the constriction of the intrahepatic veins accounts in large degree for increase in hepatic vascular resistance. These findings cause a cumulative incarceration of blood in the portal system which in turn nullifies the effectiveness of blood given to restore adequate circulating volume.—*I. R. Berger, M.D.*

Coman, Dale Rex, and DeLong, Robert P. The role of the vertebral venous system in the metastasis of cancer to the spinal column. *Cancer*, May 1951, *4*, 610–618.

From previous laboratory animal experiments the authors have concluded that the anatomical distribution of metastases depends chiefly upon the availability of tumor cell emboli rather than upon the variation in susceptibility of different organs to the growth of secondary tumors. In this study, viable tumor cell suspensions of Walker rat carcinoma 256 and V-2 carcinoma were injected into the femoral veins of rats and rabbits while slight abdominal pressure was applied. Similar control experiments were carried out on rats and rabbits without accompanying abdominal compression.

At autopsy, tumor cells were found in the vertebral venous system of 12 out of 14 rats and 4 out of 7 rabbits. Metastases were also found in the lungs, venae vasorum of the femoral vessels, the choroid plexus of the brain and less commonly in the spinal cord itself. In the control animals, with only 1 exception, metastatic tumors appeared in the lungs only.

The authors give an excellent illustrated and diagrammatic demonstration of the vertebral venous system in the rat and show the remarkable anastomoses between the vertebral and caval venous sys-

tems in the cephalic, thoracic and pelvic regions. In view of the rich intercommunication between the vertebral venous system and the dural sinuses, deep veins of the skull and orbit, the subclavian and shoulder girdle veins, the azygos system which receives tributaries from the intercostal veins, and the pelvic veins, it is readily apparent that embolic cells from primary neoplasms located in the pelvis can gain entrance to this system and be transported to the lumbar vertebrae, pelvic bones and skull. Experiments are now in progress to determine whether or not neoplasms of the breast and thyroid may metastasize by this route also.

These findings support the concept that tumor cells entering the pelvic veins may reach the lumbar vertebrae directly by way of the vertebral venous system, by passing the lungs, since no tumor foci were found in the arterioles in the areas of spontaneous vertebral column metastasis.—*J. A. Campbell, M.D.*

Sonnenblick, B. P., Levinson, Louis J., Furst, N. J., and Koch, James. The roentgen output of fluoroscopes in routine diagnostic practice. *J. Newark Beth Israel Hosp.*, July, 1951, *2*, 153–163.

The authors describe their experience during a survey of fluoroscopic installations in routine diagnostic practice. The units were in northern New Jersey, with 7 in three institutions (two hospitals and a Department of Health Clinic), and the remainder in the offices of general practitioners, radiologists, pediatricians, gastroenterologists and internists. Sixty-three units were appraised.

The dangers inherent in indiscriminate roentgenoscopy are again underlined.

The Braestrup thimble ionization chamber reading 12 r per full scale deflection was used. The measurements were in air at the "panel" which is taken to mean at the table top. All the measurements were made employing the factors ordinarily used by the operator of any particular machine. The average output was 23.6 r in air. There was no added filtration. Measurements ranged from 2 r with 65 kv. p. and 1 ma. in a radiologist's office in the examination of a child to 14.7 r with 70 kv. p. and 4 ma. in the examination of a heavy adult; 43.8 r in a pediatrician's office in the examination of a child wherein the kv. p. was not known by the pediatrician and the current was 5 ma. In the screening of a heavier older child, the output was 116.0 r where the kv. p. was not known and the current was 12.5 ma. In this latter instance the target panel distance was found to be 7.5 inches and there was an inherent filtration of 0.5 mm. Al. The distance was increased to 12 inches and the filtration raised to a total 2.0 mm. Al, reducing the output to 15 r per minute.

The fluoroscopes operated by the radiologists gave an output ranging from 5 to 28 r; the gastroenterologists ranging from 16 to 29 r; the pediatricians from 3 to 46 r, and the internists (including general practitioners) from 9 to 118 r.

The following observations were made: Many of the operators were not in the least conversant with fluoroscopic protocol. Some were careless in protection habits; none knew the output of their machines; some did not bother to accommodate but merely increased the milliamperage, kilovoltage, or both. Despite the incessant teaching and warnings about radiation damage and the modern availability of means to reduce where necessary poorly set up installations, there were some men approached by the surveyors who were willing to laugh off irradiation sequelae from the low voltage fluoroscopic work.

This is a very timely article.

It must be said that as a whole the radiologists approached by the authors were operating machines not likely to cause damage in a routine diagnostic practice.—*F. W. O'Brien, Jr., M.D.*

Van Allen, Willard W. Secondary radiation fields surrounding photofluorographic equipment. *Radiology*, June, 1951, *56*, 832–841.

Using an integrating roentgen exposure meter with a specially constructed chamber (range 0.01 to 3.0 milliroentgens) field intensities about both fixed and portable photofluorographic installations of the U. S. Public Health Service were determined. These data were used to calculate the total dosage received per week by the personnel of these installations. Such installations were found safe for normal usage but the sharp gradients make it imperative that the operator be completely shielded by the protective barrier during the exposure.—*M. B. Goodwin, M.D.*